```
$%%2)ialog;HighlightOn=%%%;HighlightOff=%%%;
Trying 9158046...Open

box200> enter system id

Logging in to Dialog



DIALOG INFORMATION SERVICES
PLEASE LOGON:
********
IALOG Invalid account number

DIALOG INFORMATION SERVICES
PLEASE LOGON:
********
ENTER PASSWORD:
x050fjxh
********
Welcome to DIALOG

Dialog level 98.04.30D

Last logoff: 18may98 07:49:09
Logon file001 18may98 08:19:44
* * * As of March 23,1998, SRC1, INFO, and EIDDS will no longer be part
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*** File 026 is not working. ***

File  1:ERIC  1966-1998/Mar
     (c) format only 1998 The Dialog Corporation

    Set  Items  Description
    ---  -----  ----------
? b 410

     18may98 08:19:48 User233832 Session D109.1
        $0.03   0.001 Hrs File1
    $0.03  Estimated cost File1
    $0.03  Estimated cost this search
    $0.03  Estimated total session cost   0.001 Hrs.

File 410:Chronolog(R)  1981-1998/May
     (c) 1998 The Dialog Corporation plc

    Set  Items  Description
    ---  -----  ----------
? set hi %%%;set hi %%%

HILIGHT set on as '%%%'%%%
%%%HILIGHT set on as '%%%'
? begin 411

     18may98 08:19:58 User233832 Session D109.2
        $0.00   0.002 Hrs File410
    $0.00  Estimated cost File410
    $0.00  Estimated cost this search
    $0.03  Estimated total session cost   0.004 Hrs.
File 411:DIALINDEX(R)

DIALINDEX(R)
  (c) 1998 The Dialog Corporation plc

*** DIALINDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAIL ON command. ***
? set files allmed allchem

   You have 174 files in your file list.
   (To see banners, use SHOW FILES command)
? s (peptide? ? or nucleic acid? ? or PNA) (6n) (fluores??????) (6n ) hapten? ?


Your SELECT statement is:
   s (peptide? ? or nucleic acid? ? or PNA) (6n) (fluores??????) (6n )
hapten? ?
      Items   File
      -----   ----
          3     5: BIOSIS PREVIEWS(R)_1969-1998/May W2
          2     6: NTIS_64-1998/Jun W2
          3    55: BIOSIS PREVIEWS(R)_1985-1998/May W2
          3    72: EMBASE_1985-1998/May W2
          4    73: EMBASE_1974-1998/May W2
          2    76: Life Sciences Collection_1982-1998/Mar
          1    94: JICST-EPlus_1985-1998/Mar W3
          4   144: Pascal_1973-1998/Apr
          1   151: HealthSTAR_1975-1998/May
         12   155: MEDLINE(R)_1966-1998/Jul W2
    Examined  50 files
          1   156: Toxline(R)_1965-1998/Feb
          1   159: Cancerlit_1975-1998/May
          1   286: Biocommerce Abs.& Dir._1981-1998/May B1
          3   348: EUROPEAN PATENTS_1978-1998/May W20
          4   351: DERWENT WPI_1963-1998/UD=9819;UP=9816;UM=9814
          1   357: Derwent Biotechnology Abs_1982-1998/May B3
          4   434: Scisearch(R) Cited Ref Sci_1974-1998/May W2
          4   440: Current Contents Search(R)_1990-1998/May W3
    Examined 100 files
         14   654: US Pat.Full._1990-1998/May 12
    Examined 150 files

  19 files have one or more items; file list includes 174 files.

? save temp hapten

Temp SearchSave "TDHAPTEN" stored
? rf

Your last SELECT statement was:
  S (PEPTIDE? ? OR NUCLEIC ACID? ? OR PNA) (6N) (FLUORES??????) (6N )
HAP-
TEN? ?
Ref      Items   File
---      -----   ----
N1          14   654: US Pat.Full._1990-1998/May 12
N2          12   155: MEDLINE(R)_1966-1998/Jul W2
N3           4    73: EMBASE_1974-1998/May W2
N4           4   144: Pascal_1973-1998/Apr
N5           4   351: DERWENT WPI_1963-1998/UD=9819;UP=9816;UM=9814
N6           4   434: Scisearch(R) Cited Ref Sci_1974-1998/May W2
N7           4   440: Current Contents Search(R)_1990-1998/May W3
N8           3     5: BIOSIS PREVIEWS(R)_1969-1998/May W2
N9           3    55: BIOSIS PREVIEWS(R)_1985-1998/May W2
N10          3    72: EMBASE_1985-1998/May W2
  19 files have one or more items; file list includes 174 files.

     - Enter P or PAGE for more -
? begin n2-n19

     18may98 08:25:39 User233832 Session D109.3
        $3.00   0.100 Hrs File411
    $3.00  Estimated cost File411
    $3.00  Estimated cost this search
    $3.03  Estimated total session cost   0.104 Hrs.

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-1998/Jul W2
     (c) format only 1998 Dialog Corporation
  File  73:EMBASE  1974-1998/May W2
     (c) 1998 Elsevier Science B.V.
  File 144:Pascal  1973-1998/Apr
     (c) 1998 INIST/CNRS
  File 351:DERWENT WPI  1963-1998/UD=9819;UP=9816;UM=9814
     (c)1998 Derwent Info Ltd
*File 351: Some images missing from UD=9816-9818 to be added as soon as
possible. Output formats changed for 1998. See HELP FORM 351 for info.
  File 434:Scisearch(R) Cited Ref Sci  1974-1998/May W2
     (c) 1998 Inst for Sci Info
  File 440:Current Contents Search(R)  1990-1998/May W3
     (c) 1998 Inst for Sci Info
  File  5:BIOSIS PREVIEWS(R)  1969-1998/May W2
     (c) 1998 BIOSIS
  File  55:BIOSIS PREVIEWS(R)  1985-1998/May W2
     (c) 1998 BIOSIS
  File  72:EMBASE  1985-1998/May W2
```

(c) 1998 Elsevier Science B.V.
File 348:EUROPEAN PATENTS 1978-1998/May W20
(c) 1998 EUROPEAN PATENT OFFICE
*File 348: *** All EPO Fulltext data is now online and current! ***
New fulltext will be added weekly. See HELP NEWS 348 for details.
File 6:NTIS 64-1998/Jun W2
Comp&distr 1998 NTIS, Intl Copyright All Righ
*File 6: NTIS has been reloaded. Accession numbers have changed.
KWIC and HILIGHT now available. RANK CS now available.
File 76:Life Sciences Collection 1982-1998/Mar
(c) 1998 Cambridge Sci Abs
File 94:JICST-EPlus 1985-1998/Mar W3
(c)1998 Japan Science and Tech Corp(JST)
File 151:HealthSTAR 1975-1998/May
(c) format only 1998 The Dialog Corporation
File 156:Toxline(R) 1965-1998/Feb
(c) format only 1998 The Dialog Corporation
File 159:Cancerlit 1975-1998/May
(c) format only 1998 Dialog Corporation
*File 159: 1998 reload availble. Accession numbers have changed.
File 286:Biocommerce Abs.& Dir. 1981-1998/May B1
(c) 1998 BioCommerce Data Ltd.
File 357:Derwent Biotechnology Abs 1982-1998/May B3
(c) 1998 Derwent Publ Ltd

Set Items Description
--- ----- -----------
? begin n1-n19

>>>Rank number "N1" does not exist
>>>"N1" is not a valid category or service name
>>>File number range must be entered as "fileno - fileno" (e.g., 12-15).
? exs

Executing TDHAPTEN
HILIGHT set on as '%'
Processing
Processed 10 of 18 files ...
Completed processing all files
2011494 PEPTIDE? ?
163584 NUCLEIC ACID? ?
19350 PNA
1218942 FLUORES??????
50443 HAPTEN? ?
S1 54 (PEPTIDE? ? OR NUCLEIC ACID? ? OR PNA) (6N)
(FLUORES??????) (6N) HAPTEN? ?
? rd

>>>Duplicate detection is not supported for File 351.
>>>Duplicate detection is not supported for File 348.
>>>Duplicate detection is not supported for File 286.

>>>Records from unsupported files will be retained in the RD set.
>>>Record 440:3017095 ignored; incomplete bibliographic data, not retained
in RD set
...examined 50 records (50)
...completed examining records
S2 27 RD (unique items)
? s (peptide? ? or nucleic acid? ? or PNA) (6n) (fluores??????) (6n) hapten? ? (12n)
synthe??????

Processing
Processing
Processed 10 of 18 files ...
Completed processing all files
2011494 PEPTIDE? ?
163584 NUCLEIC ACID? ?
19350 PNA
1218942 FLUORES??????
50443 HAPTEN? ?
4808271 SYNTHE??????
S3 9 (PEPTIDE? ? OR NUCLEIC ACID? ? OR PNA) (6N)
(FLUORES??????) (6N) HAPTEN? ? (12N) SYNTHE??????
? t s3/3,ab,k/1-9

3/3,AB,K/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

09082056 97282443
Analysis of the intracellular processing of proteins: application of fluorescence polarization and a novel fluorescent probe.
Weaver DJ Jr; Durack G; Voss EW Jr
Department of Microbiology, University of Illinois at Urbana-Champaign, Urbana 61801, USA.
Cytometry (UNITED STATES) May 1 1997, 28 (1) p25-35, ISSN 0196-4763 Journal Code: D92
Contract/Grant No.: RR03155-01, RR, NCRR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Previous studies indicated that fluorescein derivatized bovine serum albumin was an ideal probe to monitor the time-dependent kinetics of antigen processing in the murine macrophage cell line J774. Whereas previous work focused on fluorescence intensity measurements, the present study relied on fluorescence polarization to dissect the local environment of the fluorescent hapten-protein within the endocytic system of the cell. A steady increase in both fluorescence intensity and fluorescence polarization of the cell population was detected for the first 100 min. However, at 100 min, a plateau in both fluorescence intensity and polarization was observed and was followed by a decrease in fluorescence polarization and a corresponding increase in fluorescence intensity. Western blot analyses revealed that the decrease in fluorescence polarization was due to proteolytic degradation of the probe within the cell. Using a combination of in vitro experiments and an additional fluorescent probe, it was determined that the initial increase in fluorescence polarization was due to movement of the probe through a pH gradient within the cell, suggestive of transport through the endocytic system. By combining fluorescence polarization, flow cytometry, and a unique fluorescent enhancement substrate, these studies represented a novel approach for monitoring intracellular trafficking and processing of proteins within macrophages.

; Cell Line; Flow Cytometry; %Fluorescein%-5-isothiocyanate; %Fluorescent% Dyes--Chemical %Synthesis%--CS; %Fluorescent% Dyes --Metabolism--ME; %Haptens%--Immunology--IM; %Haptens%--Metabolism--ME; Macrophages--Metabolism--ME; Mice; %Peptide% Peptidohydrolases--Metabolism --ME; Polylysine--Immunology--IM; Polylysine--Metabolism--ME; Serum Albumin, Bovine--Immunology--IM; Serum...

3/3,AB,K/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

07440881 92133760
Preparation and application of a fluorescein-labeled peptide for determining the affinity constant of a monoclonal antibody-hapten complex by fluorescence polarization.
Jiskoot W; Hoogerhout P; Beuvery EC; Herron JN; Crommelin DJ
Department of Pharmaceutics, University of Utrecht, The Netherlands.
Anal Biochem (UNITED STATES) Aug 1 1991, 196 (2) p421-6, ISSN 0003-2697 Journal Code: 4NK
Contract/Grant No.: AT22898
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A simple and rapid method for determining the affinity constant of a monoclonal antibody-peptide complex under equilibrium conditions is presented. A peptide corresponding to sequence 178-185 of meningococcal strain MC50 class 1 outer membrane protein, which is recognized by monoclonal antibody MN12 (mouse IgG2a), was synthesized. After fluorescein was coupled to the peptide, the peptide-fluorescein conjugate was used for binding studies with MN12, employing fluorescence polarization of the fluorescein label to probe the bound fraction of the peptide. Scatchard analysis showed that the affinity constant was pH dependent. Storage of MN12 under alkaline conditions resulted in a loss of antigen-binding sites, but did not alter the affinity constant. Sips plots showed a homogeneity index of unity.

Descriptors: Antibodies, Monoclonal--Immunology--IM; *%Fluoresceins%; * %Haptens%--Immunology--IM; *%Peptides%--Chemical %Synthesis%--CS

3/3,AB,K/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

04028487 84179107
Covalent linkage of a synthetic peptide to a fluorescent phospholipid and its incorporation into supported phospholipid monolayers.

Thompson NL; Brian AA; McConnell HM
Biochim Biophys Acta (NETHERLANDS) Apr 25 1984, 772 (1) p10-9, ISSN 0006-3002 Journal Code: A0W
Contract/Grant No.: 5R01 AI13587, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE

A number of fluorescent %peptide%-lipid conjugates have been %synthesized%. %Peptides% with ten or eleven amino acids are linked through a single lysine residue to the headgroup of phosphatidylethanolamine, %fluorescently% labelled on one acyl chain, using homobifunctional disuccinimidyl crosslinking reagents. %Peptide% -lipids can be further derivatized with the %hapten% dinitrophenyl. Purified %peptide%-lipids have been incorporated into dimyristoylphosphatidylcholine monolayers at the interface of air and phosphate-buffered saline, at concentrations of up to 11 mol%. For equal average molecular areas, monolayers containing peptide-lipids have higher surface pressures than pure lipid monolayers; for equal surface pressures, peptide-lipid monolayers have higher average molecular areas than pure lipid monolayers. When the peptide-lipid monolayers are transferred to hydrophobic glass slides, the fluorescence appears uniformly distributed. Fluorescence recovery after photobleaching measurements indicate that peptide-lipids diffuse in the monolayer with coefficient 1.5 X 10(-9) cm2/s, which is much smaller than that of typical lipids in fluid membranes. In addition, the diffusion coefficient of peptide-lipids decreases with increasing peptide-lipid concentration. We conclude that the peptide portion of the peptide-lipid associates with the lipid monolayer and/or that peptide-lipids oligomerize.

A number of fluorescent %peptide%-lipid conjugates have been %synthesized%. %Peptides% with ten or eleven amino acids are linked through a single lysine residue to the headgroup of phosphatidylethanolamine, %fluorescently% labelled on one acyl chain, using homobifunctional disuccinimidyl crosslinking reagents. %Peptide% -lipids can be further derivatized with the %hapten% dinitrophenyl. Purified %peptide%-lipids have been incorporated into dimyristoylphosphatidylcholine monolayers at the interface of air and phosphate-buffered...

3/3,AB,K/4 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)
(c) 1998 BIOSIS. All rts. reserv.

4501917 BIOSIS Number: 78075740
COVALENT LINKAGE OF A SYNTHETIC PEPTIDE TO A FLUORESCENT PHOSPHO LIPID AND ITS INCORPORATION INTO SUPPORTED PHOSPHO LIPID MONO LAYERS
THOMPSON N L; BRIAN A A; MCCONNELL H M
DEP. CHEM., STANFORD UNIV., STANFORD, CALIF. 94305, USA.
BIOCHIM BIOPHYS ACTA 772 (1). 1984. 10-19. CODEN: BBACA
Full Journal Title: Biochimica et Biophysica Acta
Language: ENGLISH

A number of fluorescent %peptide%-lipid conjugates were %synthesized%. %Peptides% with 10 or 11 amino acids are linked through a single lysine residue to the headgroup of phosphatidylethanolamine, %fluorescently% labeled on 1 acyl chain, using homobifunctional disuccinimidyl crosslinking reagents. %Peptide%-lipids can be further derivatized with the %hapten% dinitrophenyl. Purified %peptide% -lipids were incorporated into dimyristoylphosphatidylcholine monolayers at the interface of air and phosphate-buffered saline, at concentrations of up to 11 mol%. For equal average molecular areas, monolayers containing peptide-lipids have higher surface pressures than pure lipid monolayers; for equal surface pressures, peptide-lipid monolayers have higher average molecular areas than pure lipid monolayers. When the peptide-lipid monolayers are transferred to hydrophobic glass slides, the fluorecence appears uniformly distributed. Fluorescence recovery after photobleaching measurements indicate that peptide-lipids diffuse in the monolayer with coefficient 1.5 .cntdot. 10-9 cm2/s, which is much smaller than that of typical lipids in fluid membranes. The diffusion coefficient of peptide-lipids decreases with increasing peptide-lipid concentration. The peptide portion of the peptide-lipid associates with the lipid monolayer and/or that peptide-lipids oligomerize. [The process of recognition among cells of the immune system is discussed.]

A number of fluorescent %peptide%-lipid conjugates were %synthesized%. %Peptides% with 10 or 11 amino acids are linked through a single lysine residue to the headgroup of phosphatidylethanolamine, %fluorescently% labeled on 1 acyl chain, using homobifunctional disuccinimidyl crosslinking reagents. %Peptide%-lipids can be further derivatized with the %hapten% dinitrophenyl. Purified %peptide% -lipids were incorporated into dimyristoylphosphatidylcholine monolayers at the interface of air and phosphate-buffered saline...

3/3,AB,K/5 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00922708
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Methods and compositions for promoting immunopotentiation
Methoden und Zusammensetzungen zur Forderung der Immunverstarkung
Procedes et compositions de promotion de l'immunopotentialisation
PATENT ASSIGNEE:
ARCH DEVELOPMENT CORPORATION, (995433), 1101 East 58th Street, The University of Chicago, Chicago, Illinois 60637, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Bluestone, Jeffrey A., Dr., Mararethen Strasse 48, CH-4102 Binnigen, (CH)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance (61531), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 839536 A1 980506 (Basic)
APPLICATION (CC, No, Date): EP 98100138 901026;
PRIORITY (CC, No, Date): US 429729 891027; US 524304 900516
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/39; A61K-039/00; C12P-021/08; A61K-035/74; C12N-005/08; C07K-016/00; C12P-021/08; C12R-001/91
ABSTRACT EP 839536 A1

This invention discloses immunopotentiating agents which stimulate an immune response. These agents are categorised into single agents that act directly, adjuvants added concurrently with the agents, or heteroconjugates. Heteroconjugate agents elicit or enhance a cellular or humoral immune response which may be specific for an epitope contained within an amino acid sequence. Enhanced hematopoieses by bone marrow stem cell recruitment was also a result of administering soime of these agents. Examples of immunopotentiating agents include monoclonal antibodies and proteins derived from microorganisms (e.g., enterotoxins) which activate T cells. One method of treatment disclosed uses only the immunopotentiating agent to stimulate the immune system. Another uses adjuvants in combination with the agent. A third method employs heteroconjugates. Heteroconjugates comprise: (a) an immunopotentiating protein which is characterised as having an ability to stimulate T cells; and (b) a second protein having an amino acid sequence which includes an epitope against which a cellular or humoral response is desired. This invention also relates to a method of preparing the heteroconjugate, and to a method of stimulating the immune system in vivo in a novel way. One route of stimulation is to activate T cells, in some instances, specific subsets of T cells, by administering heteroconjugates containing an immunopotentiating protein and a second protein, to mammals. For this method of treatment, the second protein in the heteroconjugate is derived from abnormal or diseased tissue, or from an infectious agent, alternatively, the second protein is produced synthetically by standard methods of molecular biology. Sources of the second protein include tumors, viruses, bacteria, fungi, protozoal or metozoal parasites. Monoclonal antibodies or T cells prepared from mammals whose immune systems have responded to administration of the heteroconjugate may be produced and administered to induce passive immunity. A method of preparing a hybridoma which secretes said monoclonal antibodies and use of these monoclonal antibodies and T cells, are also disclosed. This invention is also directed to a vaccine comprising the heteroconjugate.
ABSTRACT WORD COUNT: 324

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS A (English) 9819 911
SPEC A (English) 9819 18435
Total word count - document A 19346
Total word count - document B 0
Total word count - documents A + B 19346
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348

...SPECIFICATION is believed due to induced hematopoesis which revitalizes the graft.

Example 9: Use of a %Hapten% or %Peptide% as a Second Protein in a Heteroconjugate or as a Combination Administered Concurrently

%Fluorescein% isothiocyanate (Sigma) or Dinitrophenol (DNP) in borate buffer, pH 8.5 for 4 hours at 22(degree)C. are examples of %haptens% tested for this purpose.

Examples of other second proteins are %synthetic% peptides of HIV,

13-23 residues long prepared by the multiple simultaneous peptide method of...

3/3,AB,K/6 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 1998 EUROPEAN PATENT OFFICE. All rts. reserv.

00454583
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Biosensors.
Biosensoren.
Biosenseurs.
PATENT ASSIGNEE:
YEDA RESEARCH AND DEVELOPMENT CO. LTD., (268945), P.O. Box 95, Rehovot
76100, (IL), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Gitler, Carlos, The Weizmann Institute of Science, 4 Meonot Brazil, Rehovot 76 100, (IL)
Yuli, Itzhak, 3 Spinoza Street, Rehovot, (IL)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, D-81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 441120 A2 910814 (Basic)
EP 441120 A3 920122
EP 441120 B1 951129
APPLICATION (CC, No, Date): EP 91100198 910108;
PRIORITY (CC, No, Date): IL 93020 900109
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/543; C12M-001/40;

ABSTRACT EP 441120 A2
Biosensors for qualitative and quantitative analysis comprise an amphipathic liquid crystalline membrane composed of a lipid bilayer attached to a recording electrode via bridging anchoring molecules. The lipid bilayer is doped with biologic or synthetic ion channels and is in continuous contact with a bulk aqueous medium on both its surfaces. The bridging anchoring molecules may contain a phospholipid moiety linked to a polyoxyalkylene chain terminated with a thiol or thioether residue.
(see image in original document)
ABSTRACT WORD COUNT: 79

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS A (English) EPABF1 445
CLAIMS B (English) EPAB95 443
CLAIMS B (German) EPAB95 420
CLAIMS B (French) EPAB95 486
SPEC A (English) EPABF1 5805
SPEC B (English) EPAB95 5846
Total word count - document A 6250
Total word count - document B 7195
Total word count - documents A + B 13445

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348

...SPECIFICATION introduced as a reactive center. It permits substitution, by direct attachment or disulfide formation, of %fluorescent% probes, %haptens% or %peptides% containing desirable epitopes, without altering the helical structure. It was protected after %synthesis% as the methyldisulfide derivative (cysteine-S-S-CH(sub 3)). On reduction, it forms a...

...SPECIFICATION introduced as a reactive center. It permits substitution, by direct attachment or disulfide formation, of %fluorescent% probes, %haptens% or %peptides% containing desirable epitopes, without altering the helical structure. It was protected after %synthesis% as the methyldisulfide derivative (cysteine-S-S-CH(sub 3)). On reduction, it forms a...

3/3,AB,K/7 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 1998 EUROPEAN PATENT OFFICE. All rts. reserv.

00307332
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Particle-stabilized epitopes for standardization and control of immunoassays.
Partikelstabilisierte Epitope zur Standardisierung und Kontrolle von Immuntests.
Epitopes stabilises par des particules pour la standardisation et le controle d'essais immunologiques.
PATENT ASSIGNEE:
THE UNIVERSITY OF ROCHESTER, (290263), Office of Research and Project Administration, 30 Administration Building, Rochester, New York 14627, (US), (applicant designated states:
AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Sparks, Charles E., 139 Tobey Road, Pittsford, NY 14534, (US)
Sparks, Janet D., 139 Tobey Road, Pittsford, NY 14534, (US)
Violante, Michael R., 668 Surrey Hill Way, Rochester, NY 14623, (US)
LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 97, NL-2587 BN 's-Gravenhage, (NL)
PATENT (CC, No, Kind, Date): EP 312173 A2 890419 (Basic)
EP 312173 A3 890809
EP 312173 B1 940209
APPLICATION (CC, No, Date): EP 88202273 881012;
PRIORITY (CC, No, Date): US 108260 871013
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/68; G01N-033/577; G01N-033/92; G01N-033/543; G01N-033/547; G01N-033/546;

ABSTRACT EP 312173 A2
A process for preparing standards and controls for immunoassays employing monoclonal antibodies. Monoclonal antibodies are used to isolate a restricted portion of an antigen containing an epitope that determines the specificity of the monoclonal antibody-antigen reaction so as to distinguish it from the antigen as a whole, following fragmentation of the complex antigen by procedures including proteolysis. Isolated epitopes are attached covalently or by physical adsorption to particles to immobilize and stabilize the epitope. The particles can be composed of iodipamide ethyl ester, polyvinyl chloride, polystyrene and other inert substances and can be chemically activated to improve epitope binding and stability. Experimental details demonstrate the binding of lipoprotein to IDE, polyvinyl chloride and polystyrene and the subsequent reaction of monoclonal antibodies to these particle-stabilized epitopes.
This process is useful particularly for measuring the lipoprotein components associated with cholesterol, and includes a monoclonal based immunoassay kit for measuring the lipoprotein components in biological fluids to assess risk related to coronary artery disease complications.

ABSTRACT WORD COUNT: 166

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 785
CLAIMS B (German) EPBBF1 778
CLAIMS B (French) EPBBF1 837
SPEC B (English) EPBBF1 8165
Total word count - document A 0
Total word count - document B 10565
Total word count - documents A + B 10565

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...SPECIFICATION the immunoassay method chosen, a labeled monoclonal antibody to sialylated Lewis(sup(x) antigen or %labeled% %sialylated% Lewis(sup(x) antigen is %used% as a reagent. The label which provides for a %detectable% signal may be chosen from a large group of alternatives, including radioisotopes, %fluorescers%, enzymes or enzyme substrates, and particles.
An antigen has two properties: (1) the %capacity% to stimulate the formation of corresponding antibodies and (2) the ability to react specifically with...

3/3,AB,K/8 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00290521
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Monoclonal antibodies to specific antigenic regions of the human immunodeficiency virus and methods for use.
Monoklonale Antikorper gegen spezifische antigene Regionen des humanen

Immundefizienzvirus und Methoden zur Verwendung.
Anticorps monoclonaux contre des regions antigeniques specifiques du virus d'immunodeficience humaine et methodes d'application.
PATENT ASSIGNEE:
GENETIC SYSTEMS CORPORATION, (519930), 3005 First Avenue, Seattle Washington 98121, (US), (applicant designated states: AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Flesher, Alan Ray, 16533 Densmore Avenue North, Seattle, WA 98133, (US)
Shriver, Mary Kathleen, 13815 North East 42nd Street, Bellevue, WA 98005, (US)
LEGAL REPRESENTATIVE:
Kinzebach, Werner, Dr. et al (6468), Patentanwalte Reitstotter, Kinzebach und Partner Postfach 86 06 49, D-81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 290893 A1 881117 (Basic)
EP 290893 B1 940518
APPLICATION (CC, No, Date): EP 88106941 880429;
PRIORITY (CC, No, Date): US 45026 870501; US 67996 870629; US 105761 871007
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/577; G01N-033/569; C12N-005/00; C12P-021/00; C12N-015/00; C12P-021/00; C12R-001/91

ABSTRACT EP 290893 A1
Monoclonal antibodies capable of binding antigenic determinants within region of the core proteins of the Human Immunodeficiency Virus and immortalized cell lines producing those monoclonal antibodies are provided. The monoclonal antibodies find use in a variety of ways, including HIV antigen detection in biological samples. Using these methods, individuals may be identified who are infected with HIV but who have not yet developed anti-HIV antibodies. The methods also find use in monitoring in vitro growth of HIV, and the efficacy of therapeutic agents and vaccines.
ABSTRACT WORD COUNT: 89

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 1091
CLAIMS B (German) EPBBF1 1117
CLAIMS B (French) EPBBF1 1241
SPEC B (English) EPBBF1 6866
Total word count - document A 0
Total word count - document B 10315
Total word count - documents A + B 10315

ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348

...SPECIFICATION for detection the antibodies may either be labeled or unlabeled. A wide variety of labels %may% be employed, such %as% radionuclides, %fluorescers%, enzymes, enzyme substrates, %enzyme% cofactors, enzyme inhibitors, ligands (particularly %haptens%), etc. Numerous types of immunoassays are available, and by way of example, some include those...

3/3,AB,K/9 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 1998 EUROPEAN PATENT OFFICE. All rts. reserv.

00245151
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Diagnostic method for gonorrhea by assay of IgA1 fragments.
Diagnostisches Verfahren fur Gonorrhoe durch Proben von IgA1-Fragmenten.
Procede diagnostique pour gonorrhee par l'essai des fragments de IgA1.
PATENT ASSIGNEE:
IMMUNOGON ASSOCIATES, (834390), 98 Cutter Mill Road Suite 484N, Great Neck New York, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;SE)
INVENTOR:
Blake, Milan, 500 East 63rd Street, New York, NY, (US)
LEGAL REPRESENTATIVE:
Lawrence, Peter Robin Broughton et al (32881), GILL JENNINGS & EVERY, Broadgate House, 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 232165 A2 870812 (Basic)
EP 232165 A3 881214
EP 232165 B1 940427
APPLICATION (CC, No, Date): EP 87300950 870203;
PRIORITY (CC, No, Date): US 826227 860205
DESIGNATED STATES: CH; DE; FR; GB; IT; LI; SE
INTERNATIONAL PATENT CLASS: G01N-033/571; G01N-033/563; G01N-033/573; G01N-033/569

ABSTRACT EP 232165 A2
Method for assay of fragments produced by the reaction between the enzyme immunoglobulin A protease and its substrate immunoglobulin A, sub-class 1 comprising immunoassay with antibodies capable of reacting specifically with neo-epitopes on the fragments thus produced. IgA1, IgAP and bacteria which secrete IgAP may be detected by the method. The assay is especially useful in the detection of Neisseria gonorrhea and in the diagnosis of gonorrhea.
ABSTRACT WORD COUNT: 71

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 560
CLAIMS B (German) EPBBF1 572
CLAIMS B (French) EPBBF1 645
SPEC B (English) EPBBF1 5508
Total word count - document A 0
Total word count - document B 7285
Total word count - documents A + B 7285
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348

...SPECIFICATION a group which can be observed, a chromophoric substrate, an enzyme, for example, or a %fluorescent% group, a radioactive group, a metal, a chemiluminescent group or a suitable antigenic group or %hapten% . In these embodiments, the reaction %between% antibody and fragment is observed by measuring this label.
In certain embodiments of the present %invention%, the immunoassay comprises enzyme inhibition immunoassay (EIIA) with %peptide% having amino acid sequence of the neo-epitope. The %peptide% may be %synthesized% chemically or biochemically. It may, for example, be a cloned IgA1 fragment, Fc or Fab...
? s s2 not s3

27 S2
9 S3
S4 23 S2 NOT S3
? t s3/3,ab/1-24

3/3,AB/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 1998 Dialog Corporation. All rts. reserv.

09082056 97282443
Analysis of the intracellular processing of proteins: application of fluorescence polarization and a novel fluorescent probe.
Weaver DJ Jr; Durack G; Voss EW Jr
Department of Microbiology, University of Illinois at Urbana-Champaign, Urbana 61801, USA.
Cytometry (UNITED STATES) May 1 1997, 28 (1) p25-35, ISSN 0196-4763
Journal Code: D92
Contract/Grant No.: RR03155-01, RR, NCRR
Languages: ENGLISH
Document type: JOURNAL ARTICLE
Previous studies indicated that fluorescein derivatized bovine serum albumin was an ideal probe to monitor the time-dependent kinetics of antigen processing in the murine macrophage cell line J774. Whereas previous work focused on fluorescence intensity measurements, the present study relied on fluorescence polarization to dissect the local environment of the fluorescent hapten-protein within the endocytic system of the cell. A steady increase in both fluorescence intensity and fluorescence polarization of the cell population was detected for the first 100 min. However, at 100 min, a plateau in both fluorescence intensity and polarization was observed and was followed by a decrease in fluorescence polarization and a corresponding increase in fluorescence intensity. Western blot analyses revealed that the decrease in fluorescence polarization was due to proteolytic degradation of the probe within the cell. Using a combination of in vitro experiments and an additional fluorescent probe, it was determined that the initial increase in fluorescence polarization was due to movement of the probe through a pH gradient within the cell, suggestive of transport through the endocytic system. By combining fluorescence polarization, flow cytometry, and a unique fluorescent enhancement substrate, these studies represented a novel approach for monitoring intracellular trafficking and processing of proteins within macrophages.

3/3,AB/2 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07440881 92133760
Preparation and application of a fluorescein-labeled peptide for determining the affinity constant of a monoclonal antibody-hapten complex by fluorescence polarization.
Jiskoot W; Hoogerhout P; Beuvery EC; Herron JN; Crommelin DJ
Department of Pharmaceutics, University of Utrecht, The Netherlands.
Anal Biochem (UNITED STATES) Aug 1 1991, 196 (2) p421-6, ISSN 0003-2697 Journal Code: 4NK
Contract/Grant No.: AT22898
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A simple and rapid method for determining the affinity constant of a monoclonal antibody-peptide complex under equilibrium conditions is presented. A peptide corresponding to sequence 178-185 of meningococcal strain MC50 class 1 outer membrane protein, which is recognized by monoclonal antibody MN12 (mouse IgG2a), was synthesized. After fluorescein was coupled to the peptide, the peptide-fluorescein conjugate was used for binding studies with MN12, employing fluorescence polarization of the fluorescein label to probe the bound fraction of the peptide. Scatchard analysis showed that the affinity constant was pH dependent. Storage of MN12 under alkaline conditions resulted in a loss of antigen-binding sites, but did not alter the affinity constant. Sips plots showed a homogeneity index of unity.

3/3,AB/3 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

04028487 84179107
Covalent linkage of a synthetic peptide to a fluorescent phospholipid and its incorporation into supported phospholipid monolayers.
Thompson NL; Brian AA; McConnell HM
Biochim Biophys Acta (NETHERLANDS) Apr 25 1984, 772 (1) p10-9, ISSN 0006-3002 Journal Code: A0W
Contract/Grant No.: 5R01 AI13587, AI, NIAID
Languages: ENGLISH
Document type: JOURNAL ARTICLE
A number of fluorescent %peptide%-lipid conjugates have been %synthesized%. %Peptides% with ten or eleven amino acids are linked through a single lysine residue to the headgroup of phosphatidylethanolamine, %fluorescently% labelled on one acyl chain, using homobifunctional disuccinimidyl crosslinking reagents. %Peptide% -lipids can be further derivatized with the %hapten% dinitrophenyl. Purified %peptide%-lipids have been incorporated into dimyristoylphosphatidylcholine monolayers at the interface of air and phosphate-buffered saline, at concentrations of up to 11 mol%. For equal average molecular areas, monolayers containing peptide-lipids have higher surface pressures than pure lipid monolayers; for equal surface pressures, peptide-lipid monolayers have higher average molecular areas than pure lipid monolayers. When the peptide-lipid monolayers are transferred to hydrophobic glass slides, the fluorescence appears uniformly distributed. Fluorescence recovery after photobleaching measurements indicate that peptide-lipids diffuse in the monolayer with coefficient 1.5 X 10(-9) cm2/s, which is much smaller than that of typical lipids in fluid membranes. In addition, the diffusion coefficient of peptide-lipids decreases with increasing peptide-lipid concentration. We conclude that the peptide portion of the peptide-lipid associates with the lipid monolayer and/or that peptide-lipids oligomerize.

3/3,AB/4 (Item 1 from file: 5)
DIALOG(R)File 5:BIOSIS PREVIEWS(R)

4501917 BIOSIS Number: 78075740
COVALENT LINKAGE OF A SYNTHETIC PEPTIDE TO A FLUORESCENT PHOSPHO LIPID
AND ITS INCORPORATION INTO SUPPORTED PHOSPHO LIPID MONO LAYERS
THOMPSON N L; BRIAN A A; MCCONNELL H M
DEP. CHEM., STANFORD UNIV., STANFORD, CALIF. 94305, USA.
BIOCHIM BIOPHYS ACTA 772 (1). 1984. 10-19. CODEN: BBACA
Full Journal Title: Biochimica et Biophysica Acta
Language: ENGLISH
A number of fluorescent %peptide%-lipid conjugates were %synthesized%. %Peptides% with 10 or 11 amino acids are linked through a single lysine residue to the headgroup of phosphatidylethanolamine, %fluorescently% labeled on 1 acyl chain, using homobifunctional disuccinimidyl crosslinking reagents. %Peptide%-lipids can be further derivatized with the %hapten% dinitrophenyl. Purified %peptide% -lipids were incorporated into dimyristoylphosphatidylcholine monolayers at the interface of air and phosphate-buffered saline, at concentrations of up to 11 mol%. For equal average molecular areas, monolayers containing peptide-lipids have higher surface pressures than pure lipid monolayers; for equal surface pressures, peptide-lipid monolayers have higher average molecular areas than pure lipid monolayers. When the peptide-lipid monolayers are transferred to hydrophobic glass slides, the fluorecence appears uniformly distributed. Fluorescence recovery after photobleaching measurements indicate that peptide-lipids diffuse in the monolayer with coefficient 1.5 .cntdot. 10-9 cm2/s, which is much smaller than that of typical lipids in fluid membranes. The diffusion coefficient of peptide-lipids decreases with increasing peptide-lipid concentration. The peptide portion of the peptide-lipid associates with the lipid monolayer and/or that peptide-lipids oligomerize. [The process of recognition among cells of the immune system is discussed.]

3/3,AB/5 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00922708
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Methods and compositions for promoting immunopotentiation
Methoden und Zusammensetzungen zur Forderung der Immunverstarkung
Procedes et compositions de promotion de l'immunopotentialisation
PATENT ASSIGNEE:
ARCH DEVELOPMENT CORPORATION, (995433), 1101 East 58th Street, The University of Chicago, Chicago, Illinois 60637, (US), (applicant designated states: AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Bluestone, Jeffrey A., Dr., Mararethen Strasse 48, CH-4102 Binnigen, (CH)
LEGAL REPRESENTATIVE:
Gowshall, Jonathan Vallance (61531), FORRESTER & BOEHMERT Franz-Joseph-Strasse 38, 80801 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 839536 A1 980506 (Basic)
APPLICATION (CC, No, Date): EP 98100138 901026;
PRIORITY (CC, No, Date): US 429729 891027; US 524304 900516
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/39; A61K-039/00; C12P-021/08; A61K-035/74; C12N-005/08; C07K-016/00; C12P-021/08; C12R-001/91
ABSTRACT EP 839536 A1
This invention discloses immunopotentiating agents which stimulate an immune response. These agents are categorised into single agents that act directly, adjuvants added concurrently with the agents, or heteroconjugates. Heteroconjugate agents elicit or enhance a cellular or humoral immune response which may be specific for an epitope contained within an amino acid sequence. Enhanced hematopoieses by bone marrow stem cell recruitment was also a result of administering soime of these agents. Examples of immunopotentiating agents include monoclonal antibodies and proteins derived from microorganisms (e.g., enterotoxins) which activate T cells. One method of treatment disclosed uses only the immunopotentiating agent to stimulate the immune system. Another uses adjuvants in combination with the agent. A third method employs heteroconjugates. Heteroconjugates comprise: (a) an immunopotentiating protein which is characterised as having an ability to stimulate T cells; and (b) a second protein having an amino acid sequence which includes an epitope against which a cellular or humoral response is desired. This invention also relates to a method of preparing the heteroconjugate, and to a method of stimulating the immune system in vivo in a novel way. One route of stimulation is to activate T cells, in some instances, specific subsets of T cells, by administering heteroconjugates containing an immunopotentiating protein and a second protein, to mammals. For this method of treatment, the second protein in the heteroconjugate is derived from abnormal or diseased tissue, or from an infectious agent, alternatively, the second protein is produced synthetically by standard methods of molecular biology. Sources of the second protein include tumors, viruses, bacteria, fungi, protozoal or metozoal parasites. Monoclonal antibodies or T cells prepared from mammals whose immune systems have responded to administration of the heteroconjugate may be produced and administered to induce passive immunity. A method of preparing a hybridoma which secretes said monoclonal antibodies and use of these monoclonal antibodies and T cells, are also disclosed. This invention is also directed to a vaccine comprising the heteroconjugate.
ABSTRACT WORD COUNT: 324

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS A (English) 9819 911
SPEC A (English) 9819 18435
Total word count - document A 19346
Total word count - document B 0
Total word count - documents A + B 19346

3/3,AB/6 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00454583
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Biosensors.
Biosensoren.
Biosenseurs.
PATENT ASSIGNEE:
YEDA RESEARCH AND DEVELOPMENT CO. LTD., (268945), P.O. Box 95, Rehovot
76100, (IL), (applicant designated states:
AT;BE;CH;DE;DK;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Gitler, Carlos, The Weizmann Institute of Science, 4 Meonot Brazil, Rehovot 76 100, (IL)
Yuli, Itzhak, 3 Spinoza Street, Rehovot, (IL)
LEGAL REPRESENTATIVE:
VOSSIUS & PARTNER (100311), Postfach 86 07 67, D-81634 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 441120 A2 910814 (Basic)
EP 441120 A3 920122
EP 441120 B1 951129
APPLICATION (CC, No, Date): EP 91100198 910108;
PRIORITY (CC, No, Date): IL 93020 900109
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/543; C12M-001/40;

ABSTRACT EP 441120 A2
Biosensors for qualitative and quantitative analysis comprise an amphipathic liquid crystalline membrane composed of a lipid bilayer attached to a recording electrode via bridging anchoring molecules. The lipid bilayer is doped with biologic or synthetic ion channels and is in continuous contact with a bulk aqueous medium on both its surfaces. The bridging anchoring molecules may contain a phospholipid moiety linked to a polyoxyalkylene chain terminated with a thiol or thioether residue.
(see image in original document)
ABSTRACT WORD COUNT: 79

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS A (English) EPABF1 445
CLAIMS B (English) EPAB95 443
CLAIMS B (German) EPAB95 420
CLAIMS B (French) EPAB95 486
SPEC A (English) EPABF1 5805
SPEC B (English) EPAB95 5846
Total word count - document A 6250
Total word count - document B 7195
Total word count - documents A + B 13445

3/3,AB/7 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00307332
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Particle-stabilized epitopes for standardization and control of immunoassays.
Partikelstabilisierte Epitope zur Standardisierung und Kontrolle von Immuntests.
Epitopes stabilises par des particules pour la standardisation et le controle d'essais immunologiques.
PATENT ASSIGNEE:
THE UNIVERSITY OF ROCHESTER, (290263), Office of Research and Project Administration, 30 Administration Building, Rochester, New York 14627, (US), (applicant designated states:
AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Sparks, Charles E., 139 Tobey Road, Pittsford, NY 14534, (US)
Sparks, Janet D., 139 Tobey Road, Pittsford, NY 14534, (US)
Violante, Michael R., 668 Surrey Hill Way, Rochester, NY 14623, (US)
LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 97, NL-2587 BN 's-Gravenhage, (NL)
PATENT (CC, No, Kind, Date): EP 312173 A2 890419 (Basic)
EP 312173 A3 890809
EP 312173 B1 940209
APPLICATION (CC, No, Date): EP 88202273 881012;
PRIORITY (CC, No, Date): US 108260 871013
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/68; G01N-033/577; G01N-033/92; G01N-033/543; G01N-033/547; G01N-033/546;

ABSTRACT EP 312173 A2
A process for preparing standards and controls for immunoassays employing monoclonal antibodies. Monoclonal antibodies are used to isolate a restricted portion of an antigen containing an epitope that determines the specificity of the monoclonal antibody-antigen reaction so as to distinguish it from the antigen as a whole, following fragmentation of the complex antigen by procedures including proteolysis. Isolated epitopes are attached covalently or by physical adsorption to particles to immobilize and stabilize the epitope. The particles can be composed of iodipamide ethyl ester, polyvinyl chloride, polystyrene and other inert substances and can be chemically activated to improve epitope binding and stability. Experimental details demonstrate the binding of lipoprotein to IDE, polyvinyl chloride and polystyrene and the subsequent reaction of monoclonal antibodies to these particle-stabilized epitopes.
This process is useful particularly for measuring the lipoprotein components associated with cholesterol, and includes a monoclonal based immunoassay kit for measuring the lipoprotein components in biological fluids to assess risk related to coronary artery disease complications.

ABSTRACT WORD COUNT: 166

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 785
CLAIMS B (German) EPBBF1 778
CLAIMS B (French) EPBBF1 837
SPEC B (English) EPBBF1 8165
Total word count - document A 0
Total word count - document B 10565
Total word count - documents A + B 10565

3/3,AB/8 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
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00290521
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Monoclonal antibodies to specific antigenic regions of the human immunodeficiency virus and methods for use.
Monoklonale Antikorper gegen spezifische antigene Regionen des humanen Immundefizienzvirus und Methoden zur Verwendung.
Anticorps monoclonaux contre des regions antigeniques specifiques du virus d'immunodeficience humaine et methodes d'application.
PATENT ASSIGNEE:
GENETIC SYSTEMS CORPORATION, (519930), 3005 First Avenue, Seattle Washington 98121, (US), (applicant designated states:
AT;BE;CH;DE;ES;FR;GB;GR;IT;LI;LU;NL;SE)
INVENTOR:
Flesher, Alan Ray, 16533 Densmore Avenue North, Seattle, WA 98133, (US)
Shriver, Mary Kathleen, 13815 North East 42nd Street, Bellevue, WA 98005, (US)
LEGAL REPRESENTATIVE:
Kinzebach, Werner, Dr. et al (6468), Patentanwalte Reitstotter, Kinzebach und Partner Postfach 86 06 49, D-81633 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 290893 A1 881117 (Basic)
EP 290893 B1 940518
APPLICATION (CC, No, Date): EP 88106941 880429;
PRIORITY (CC, No, Date): US 45026 870501; US 67996 870629; US 105761 871007
DESIGNATED STATES: AT; BE; CH; DE; ES; FR; GB; GR; IT; LI; LU; NL; SE
INTERNATIONAL PATENT CLASS: G01N-033/577; G01N-033/569; C12N-005/00; C12P-021/00; C12N-015/00; C12P-021/00; C12R-001/91

ABSTRACT EP 290893 A1

Monoclonal antibodies capable of binding antigenic determinants within region of the core proteins of the Human Immunodeficiency Virus and immortalized cell lines producing those monoclonal antibodies are provided. The monoclonal antibodies find use in a variety of ways, including HIV antigen detection in biological samples. Using these methods, individuals may be identified who are infected with HIV but who have not yet developed anti-HIV antibodies. The methods also find use in monitoring in vitro growth of HIV, and the efficacy of therapeutic agents and vaccines.
ABSTRACT WORD COUNT: 89

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 1091
CLAIMS B (German) EPBBF1 1117
CLAIMS B (French) EPBBF1 1241
SPEC B (English) EPBBF1 6866
Total word count - document A 0
Total word count - document B 10315
Total word count - documents A + B 10315

3/3,AB/9 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS
(c) 1998 EUROPEAN PATENT OFFICE. All rts. reserv.

00245151
ORDER fax of complete patent from Dialog SourceOne. See HELP ORDER 348
Diagnostic method for gonorrhea by assay of IgA1 fragments.
Diagnostisches Verfahren fur Gonorrhoe durch Proben von IgA1-Fragmenten.
Procede diagnostique pour gonorrhee par l'essai des fragments de IgA1.
PATENT ASSIGNEE:
IMMUNOGON ASSOCIATES, (834390), 98 Cutter Mill Road Suite 484N, Great Neck New York, (US), (applicant designated states: CH;DE;FR;GB;IT;LI;SE)
INVENTOR:
Blake, Milan, 500 East 63rd Street, New York, NY, (US)
LEGAL REPRESENTATIVE:
Lawrence, Peter Robin Broughton et al (32881), GILL JENNINGS & EVERY, Broadgate House, 7 Eldon Street, London EC2M 7LH, (GB)
PATENT (CC, No, Kind, Date): EP 232165 A2 870812 (Basic)
EP 232165 A3 881214
EP 232165 B1 940427
APPLICATION (CC, No, Date): EP 87300950 870203;
PRIORITY (CC, No, Date): US 826227 860205
DESIGNATED STATES: CH; DE; FR; GB; IT; LI; SE
INTERNATIONAL PATENT CLASS: G01N-033/571; G01N-033/563; G01N-033/573; G01N-033/569

ABSTRACT EP 232165 A2
Method for assay of fragments produced by the reaction between the enzyme immunoglobulin A protease and its substrate immunoglobulin A, sub-class 1 comprising immunoassay with antibodies capable of reacting specifically with neo-epitopes on the fragments thus produced. IgA1, IgAP and bacteria which secrete IgAP may be detected by the method. The assay is especially useful in the detection of Neisseria gonorrhea and in the diagnosis of gonorrhea.
ABSTRACT WORD COUNT: 71

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:
Available Text Language Update Word Count
CLAIMS B (English) EPBBF1 560
CLAIMS B (German) EPBBF1 572
CLAIMS B (French) EPBBF1 645
SPEC B (English) EPBBF1 5508
Total word count - document A 0
Total word count - document B 7285
Total word count - documents A + B 7285
? begin 654

18may98 08:33:37 User233832 Session D109.4
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$1.20 6 Type(s) in Format 4 (UDF)
$1.20 6 Types
$1.53 Estimated cost File155
$0.72 0.008 Hrs File73
$0.72 Estimated cost File73
$0.99 0.022 Hrs File144
$0.99 Estimated cost File144
$1.10 0.005 Hrs File351
$1.10 Estimated cost File351
$0.99 0.011 Hrs File434
$0.99 Estimated cost File434
$0.45 0.006 Hrs File440
$0.45 Estimated cost File440
$0.60 0.010 Hrs File5
$2.90 2 Type(s) in Format 5 (UDF)
$2.90 2 Types
$3.50 Estimated cost File5
$0.36 0.006 Hrs File55
$0.36 Estimated cost File55
$0.54 0.006 Hrs File72
$0.54 Estimated cost File72
$1.44 0.016 Hrs File348
$50.00 10 Type(s) in Format 5 (UDF)
$50.00 10 Types
$51.44 Estimated cost File348
$0.06 0.001 Hrs File6
$0.06 Estimated cost File6
$0.30 0.005 Hrs File76
$0.30 Estimated cost File76
$0.18 0.004 Hrs File94
$0.18 Estimated cost File94
$0.06 0.002 Hrs File151
$0.06 Estimated cost File151
$0.18 0.006 Hrs File156
$0.18 Estimated cost File156
$0.09 0.003 Hrs File159
$0.09 Estimated cost File159
$0.06 0.001 Hrs File286
$0.06 Estimated cost File286
$0.27 0.002 Hrs File357
$0.27 Estimated cost File357
OneSearch, 18 files, 0.133 Hrs FileOS
$62.82 Estimated cost this search
$65.85 Estimated total session cost 0.237 Hrs.

File 654:US Pat.Full. 1990-1998/May 12
(c) format only 1998 The Dialog Corp.
*File 654: Reassignment data now current through 03/24/98.
Reexamination, extension, expiration, reinstatement updated weekly.

Set Items Description
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? s (peptide? ? or nucleic acid? ? or PNA) (6n) (fluores??????) (6n) hapten? ?

20495 PEPTIDE? ?
0 NUCLEIC ACID? ?
742 PNA
32598 FLUORES??????
2641 HAPTEN? ?
S1 14 (PEPTIDE? ? OR NUCLEIC ACID? ? OR PNA) (6N) (FLUORES??????) (6N) HAPTEN? ?
? t s1/3,ab/1-14

1/3,AB/1
DIALOG(R)File 654:US Pat.Full.
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02770562
Utility
NUCLEOTIDE-DIRECTED ASSEMBLY OF BIMOLECULAR AND MULTIMOLECULAR DRUGS AND DEVICES

PATENT NO.: 5,739,305
ISSUED: April 14, 1998 (19980414)
INVENTOR(s): Cubicciotti, Roger S., 258 Midland Ave., Montclair, NJ (New Jersey), US (United States of America), 07042 68000]
APPL. NO.: 8-487,968
FILED: June 07, 1995 (19950607)

This is a division of application Ser. No. 08-169,517, filed Dec. 17, 1993 now abandoned.

FULL TEXT: 1481 lines

ABSTRACT

Methods of producing synthetic heteropolymers and multivalent heteropolymeric hybrid structures capable of assembling non-oligonucleotide molecules are provided. These structures are used to direct the assembly of multimolecular complexes. A number of synthetic heteropolymers, multivalent heteropolymeric hybrid structures and multimolecular complexes are also provided.

1/3,AB/2
DIALOG(R)File 654:US Pat.Full.

02756212
Utility
LOCALIZATION AND CHARACTERIZATION OF THE WILMS' TUMOR GENE

PATENT NO.: 5,726,288
ISSUED: March 10, 1998 (19980310)
INVENTOR(s): Call, Katherine M., Malden, MA (Massachusettes), US (United States of America)
Glaser, Thomas M., Belmont, MA (Massachusettes), US (United States of America)
Ito, Caryn Y., Chapel Hill, NC (North Carolina), US (United States of America)
Buckler, Alan J., Cambridge, MA (Massachusettes), US (United States of America)
Pelletier, Jerry, Montreal, CA (Canada)
Haber, Daniel A., Cambridge, MA (Massachusettes), US (United States of America)
Rose, Elise A., Oakland, CA (California), US (United States of America)
Housman, David E., Newton, MA (Massachusettes), US (United States of America)
Bruening, Wendy, Montreal, CA (Canada)
Darveau, Andre, St. Foy, CA (Canada)
ASSIGNEE(s): Massachusetts Institute of Technology, (A U.S. Company or Corporation), Cambridge, MA (Massachusetts), US (United States of America)
[Assignee Code(s): 52912]
APPL. NO.: 8-102,942
FILED: August 02, 1993 (19930802)

The present application is a continuation-in-part of U.S. Ser. No. 07-614,161, filed Nov. 13, 1990, now abandoned, which is a continuation-in-part of U.S. Ser. No. 07-435,780 filed on Nov. 13, 1989, now abandoned, the contents of which are herein incorporated by reference.

FULL TEXT: 1898 lines

ABSTRACT

The Wilms' tumor gene associated with 11p3 locus on the human chromosome, as well as a method of analyzing cells for the gene is described and characterized. The gene encodes a transcription unit approximately 50 kb in size and a mRNA of approximately 3 kb, which is expressed in predominantly in kidney and gonadal tissue. The gene is alternative spliced producing four very similar mRNA transcripts. The polypeptides encoded by the Wilms' tumor DNA includes four "zinc fingers" and a region rich in proline and glutamine, suggesting that the polypeptide has a role in transcription regulation.

1/3,AB/3
DIALOG(R)File 654:US Pat.Full.

02677860
Utility
NUCLEOTIDE-DIRECTED ASSEMBLY OF BIMOLECULAR AND MULTIMOLECULAR DRUGS AND DEVICES

PATENT NO.: 5,656,739
ISSUED: August 12, 1997 (19970812)
INVENTOR(s): Cubicciotti, Roger S., 258 Midland Ave., Montclair, NJ (New Jersey), US (United States of America), 07042 68000]
APPL. NO.: 8-487,959
FILED: June 07, 1995 (19950607)

This is a divisional of application Ser. No. 08-169,517, filed Dec. 17, 1993.

FULL TEXT: 1575 lines

ABSTRACT

Methods of producing synthetic heteropolymers and multivalent heteropolymeric hybrid structures capable of assembling non-oligonucleotide molecules are provided. These structures are used to direct the assembly of multimolecular complexes. A number of synthetic heteropolymers, multivalent heteropolymeric hybrid structures and multimolecular complexes are also provided.

1/3,AB/4
DIALOG(R)File 654:US Pat.Full.

02672721
Utility
YC1 GENE

PATENT NO.: 5,652,144
ISSUED: July 29, 1997 (19970729)
INVENTOR(s): Lu, Yinchen, Wellesley, MA (Massachusettes), US (United States of America)
Haseltine, William A., Cambridge, MA (Massachusettes), US (United States of America)
ASSIGNEE(s): Dana-Farber Cancer Institute, (A U.S. Company or Corporation), Boston, MA (Massachusetts), US (United States of America)
[Assignee Code(s): 11804]
APPL. NO.: 7-973,431
FILED: November 10, 1992 (19921110)

FULL TEXT: 1460 lines

ABSTRACT

Isolated and purified YC1 genes and proteins are disclosed. The protein binds to a site in the HIV-LTR, the NRE-1 site, and can inhibit the expression of a gene operably linked to the HIV-1 LTR. The use of the protein and gene are discussed. Repressible and inducible expression systems using the YC1 gene are also disclosed.

1/3,AB/5
DIALOG(R)File 654:US Pat.Full.

02629978
Utility
ANTIBODY TO PNA/NUCLEIC ACID COMPLEXES

PATENT NO.: 5,612,458
ISSUED: March 18, 1997 (19970318)
INVENTOR(s): Hyldig-Nielsen, Jens J., Vanl.o slashed.se, DK (Denmark)
Pluzek, Karl-Johan, Smoerum, DK (Denmark)
ASSIGNEE(s): Dako/AS, (A Non-U.S. Company or Corporation), DK (Denmark)
[Assignee Code(s): 41353]
APPL. NO.: 8-361,643
FILED: December 22, 1994 (19941222)
PRIORITY: 1454-93, DK (Denmark), December 23, 1993 (19931223)

FULL TEXT: 885 lines

ABSTRACT

This invention relates to antibodies to complexes formed between PNA (Peptide Nucleic Acid) and nucleic acids, particularly antibodies to PNA/DNA or PNA/RNA complexes. The preferred antibodies are polyclonal, monoclonal and recombinant antibodies that binds to PNA/DNA or PNA/RNA complexes, but not to single-stranded PNA, double-stranded nucleic acid or single-stranded nucleic acid. Peptide Nucleic Acids (PNA) are newly

developed, not naturally occurring compounds comprising a polyamide backbone bearing a plurality of ligands such as naturally occuring nucleobases attached to a polyamide backbone through a suitable linker. PNA oligomers with a backbone of N-(2-aminoethyl)glycin units have a surprising high affinity for complementary nucleic acid forming very stable and specific complexes. This property makes PNA oligomers suitable as hybridization probes for detection of nucleic acids. The usability of PNA as hybridization probes is greatly increased by the present antibodies. The antibodies according to the invention are useful in the capture, recognition, detection, identification or quantitation of nucleic acids in biological samples, via their ability to react with PNA-nucleic acid complexes.

1/3,AB/6
DIALOG(R)File 654:US Pat.Full.
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02542987
Utility
METHOD FOR REGULATING FORMATION OF A COMPLEX OF PLASMINOGEN ACTIVATOR, ITS
RECEPTOR AND INHIBITOR
[Screening for a test of cells with tissue plasminogen activator]

PATENT NO.: 5,532,132
ISSUED: July 02, 1996 (19960702)
INVENTOR(s): Wang, Ning, Wuhan, CN (China)
Barlovatz-Meimon, Georgia, Paris, FR (France)
Fredberg, Jeffrey J., Sharon, MA (Massachusettes), US (United States of America)
ASSIGNEE(s): President and Fellows of Harvard University, (A U.S. Company or Corporation), Cambridge, MA (Massachusetts), US (United States of America)
University of Paris, (A Non-U.S. Company or Corporation), FR (France)
[Assignee Code(s): 542; 12991]
APPL. NO.: 8-127,977
FILED: September 28, 1993 (19930928)
The United States Government has rights in this invention by virtue of the National Heart, Lung and Blood Institute grant P01 HL 33009.

FULL TEXT: 886 lines

ABSTRACT

The present invention is directed to a method for regulating formation of a complex of a plasminogen activator, its receptor and one of its inhibitors. More specifically, this method involves contacting a target cell having a plasminogen activator receptor with a compound which interacts with a component of the complex such that a change in target cell cytoskeletal stiffness results.

1/3,AB/7
DIALOG(R)File 654:US Pat.Full.
(c) format only 1998 The Dialog Corp. All rts. reserv.

02531049
Utility
BIOTINYLATION REAGENT AND METHOD OF USE THEREOF

PATENT NO.: 5,521,319
ISSUED: May 28, 1996 (19960528)
INVENTOR(s): Huber, Erasmus, St. Willibald 10, D-86923 Finning, DE (Germany)
Zink, Bruno, Seeblickstrasse 4, D-82449 Uffing, DE (Germany)
Lenz, Helmut, Von-Kuhlmann-Strasse 14, D-82327 Tutzing, DE (Germany)
Hoess, Eva, Am Muhlberg 1a, D-82319 Starnberg, DE (Germany)
68000]
EXTRA INFO: Assignment transaction [Reassigned], recorded September 14, 1994 (19940914)
APPL. NO.: 8-295,793
FILED: September 14, 1994 (19940914)
PRIORITY: 43-02-241.3, DE (Germany), January 27, 1993 (19930127) ok
PCT: PCT-EP94-00195 (WO 94EP195)
Section 371 Date: September 14, 1994 (19940914)
Section 102(e) Date: September 14, 1994 (19940914)
Filing Date: January 25, 1994 (19940125)
Publication Number: WO94-17072 (WO 9417072)
Publication Date: August 04, 1994 (19940804)

FULL TEXT: 477 lines

ABSTRACT

The invention concerns a compound of the general formula (I): [See structure in original document] in which Bi denotes a residue derived by cleavage of a carboxyl group from biotin or from a biotin derivative, R sup 1 and R sup 2 denote independently of one another hydrogen or C sub 1 --C sub 4 alkyl,

n denotes an integer from 4 to 10 and

X denotes an alkylene residue with a chain length of 5 to 20 atoms substituted by one or several O or/and S atoms and a conjugate of this compound with a substance that has at least one primary or/and secondary amino group NHR sup 3.

1/3,AB/8
DIALOG(R)File 654:US Pat.Full.
(c) format only 1998 The Dialog Corp. All rts. reserv.

02468383
Utility
SEQUENTIAL OLIGONUCLEOTIDE SYNTHESES USING IMMUNOAFFINITY TECHNIQUES

PATENT NO.: 5,464,759
ISSUED: November 07, 1995 (19951107)
INVENTOR(s): Coolidge, Thomas R., Falls Village, CT (Connecticut), US (United States of America)
Lewis, William, Lincoln, NE (Nebraska), US (United States of America)
Schuster, Sheldon M., Gainesville, FL (Florida), US (United States of America)
Stout, Jay, Lincoln, NE (Nebraska), US (United States of America)
van Heeke, Gino, Gainesville, FL (Florida), US (United States of America)
Wylie, Dwane, Lincoln, NE (Nebraska), US (United States of America)
Wagner, Fred W., Walton, NE (Nebraska), US (United States of America)
ASSIGNEE(s): BioNebraska, Inc, (A U.S. Company or Corporation), Lincoln, NE (Nebraska), US (United States of America)
Board of Regents of the University of Nebraska, (A U.S. Company or Corporation), Lincoln, NE (Nebraska), US (United States of America)
[Assignee Code(s): 31099; 58949]
APPL. NO.: 8-18,100
FILED: February 17, 1993 (19930217)

This is a division, of application Ser. No. 07454,372, filed Dec. 21, 1989, now U.S. Pat. No. 5,221,736; which is a continuation-in-part of application Ser. No. 07-288,009 filed, Dec. 12, 1988, now U.S. Pat. No. 5,049,656.

FULL TEXT: 1423 lines

ABSTRACT

The invention is directed to a method of purifying sequentially synthesized peptides and oligonucleotides by affinity techniques. Selected products are capped with and N-terminus capping agent for peptides or a 5'-terminus capping agents for oligonucleotides, and then bound with affinity agents that are selective for the corresponding capping agents.

1/3,AB/9
DIALOG(R)File 654:US Pat.Full.
(c) format only 1998 The Dialog Corp. All rts. reserv.

02433980
Utility
DIBENZOPYRROMETHENEBORON DIFLUORIDE DYES [FLUORESCENT]

PATENT NO.: 5,433,896
ISSUED: July 18, 1995 (19950718)
INVENTOR(s): Kang, Hee C., Eugene, OR (Oregon), US (United States of America)
Haugland, Richard P., Eugene, OR (Oregon), US (United States of America)
ASSIGNEE(s): Molecular Probes, Inc, (A U.S. Company or Corporation), Eugene , OR (Oregon), US (United States of America)
[Assignee Code(s): 19082]
APPL. NO.: 8-246,790
FILED: May 20, 1994 (19940520)

FULL TEXT: 1065 lines

ABSTRACT

The invention relates to fluorescent dyes that are substituted or unsubstituted derivatives of 1-[isoindolyl]methylene-isoindole that are bound through both isoindole nitrogens to a boron difluoride moiety, forming a fluorescent dibenzopyrromethenebaron difluoride compound [See structure in original document] whose fluorescence properties are modified by the selection of appropriate chemical substituents.

The dibenzopyrromethenebaron difluoride compound is optionally substituted by hydrogen, halogen cyano, sulfo, alkali or ammonium salts of sulfo, carboxy, substituted or unsubstituted alkyl, perfluoroalkyl, alkoxy, alkylthio, nitro, amino, monoalkylamino, dialkylamino, substituted or unsubstituted aryl substituents, substituted or unsubstituted heteroaryl substituents, or additional substituted or unsubstituted fused benzo rings or substituted or unsubstituted fused heteroaromatic rings. Any alkyl substituent present on the subject dye is optionally further substituted by a reactive site, or a functional group that can be readily converted into a reactive site.

1/3,AB/10
DIALOG(R)File 654:US Pat.Full.

02361686
Utility
ANTIBODIES FOR P-GLYCOPROTEIN ENCODED BY THE MDR1 GENE AND USES THEREOF

PATENT NO.: 5,369,009
ISSUED: November 29, 1994 (19941129)
INVENTOR(s): Arceci, Robert J., Westwood, MA (Massachusettes), US (United States of America)
Croop, James M., Jamaica Plain, MA (Massachusettes), US (United States of America)
ASSIGNEE(s): Dana Farber Cancer Institute, (A U.S. Company or Corporation), Boston, MA (Massachusetts), US (United States of America)
[Assignee Code(s): 11804]
APPL. NO.: 7-870,627
FILED: April 17, 1992 (19920417)

FULL TEXT: 829 lines

ABSTRACT

A novel antibody capable of binding to a 170,000 dalton P-glycoprotein encoded by the mdr1 gene, wherein said antibody binds to an external epitope on the protein and does not substantially increase the intracellular accumulaton or the cytoxicity of either Daunomycin or vinblastine in multidrug resistant cells is described. Methods of use of such antibodies are also described.

1/3,AB/11
DIALOG(R)File 654:US Pat.Full.

02195760
Utility
SEQUENTIAL PEPTIDE AND OLIGONUCLEOTIDE SYNTHESES USING IMMUNOAFFINITY
TECHNIQUES
[Blocking, capping. deblocking 3'- and 5'-nucleotides, forming polynucleotides; purifying by affinity techniques]

PATENT NO.: 5,221,736
ISSUED: June 22, 1993 (19930622)
INVENTOR(s): Coolidge, Thomas R., Falls Village, CT (Connecticut), US (United States of America)
Lewis, William, Lincoln, NE (Nebraska), US (United States of America)
Schuster, Sheldon M., Gainesville, FL (Florida), US (United States of America)
Wylie, Dwane, Lincoln, NE (Nebraska), US (United States of America)
Wagner, Fred W., Walton, NE (Nebraska), US (United States of America)
Stout, Jay, Lincoln, NE (Nebraska), US (United States of America)
van Heeke, Gino, Gainesville, FL (Florida), US (United States of America)
ASSIGNEE(s): BioNebraska, Inc , (A U.S. Company or Corporation), Lincoln, NE (Nebraska), US (United States of America)
Board of Regents of the University of Nebraska, (A U.S. Company or Corporation), Lincoln, NE (Nebraska), US (United States of America)
[Assignee Code(s): 31099; 58949]
APPL. NO.: 7-454,372
FILED: December 21, 1989 (19891221)

CROSS-REFERENCE TO RELATED APPLICATIONS

This patent application is a continuation-in-part of U.S. application Ser. No. 288,009, filed Dec. 21, 1988, which has issued as U.S. Pat. No. 5,049,656.

FULL TEXT: 1663 lines

ABSTRACT

The invention is directed to a method of purifying sequentially synthesized peptides and oligonucleotides by affinity techniques. Selected products are capped with and N-terminus capping agent for peptides or a 5'-terminus capping agents for oligonucleotides, and then bound with affinity agents that are selective for the corresponding capping agents.

1/3,AB/12
DIALOG(R)File 654:US Pat.Full.

02186970
Utility
ASSAY FOR POLYOMAVIRUS IN HUMANS AND USES THEREOF

PATENT NO.: 5,213,796
ISSUED: May 25, 1993 (19930525)
INVENTOR(s): Garcea, Robert L., Wellesley, MA (Massachusettes), US (United States of America)
Bergsagel, Daniel J., Arlington, MA (Massachusettes), US (United States of America)
ASSIGNEE(s): Dana Farber Cancer Institute, (A U.S. Company or Corporation), Boston, MA (Massachusettes), US (United States of America)
[Assignee Code(s): 11804]
APPL. NO.: 7-695,647
FILED: May 06, 1991 (19910506)

FULL TEXT: 732 lines

ABSTRACT

Methods for detecting the propensity for an individual to be affected by a polyomavirus are disclosed. The methods include an assay wherein a biological specimen from a female is contacted with at least one probe capable of determining whether the female has been exposed to a polyomavirus. A method for prophylactically treating the female is also described.

1/3,AB/13
DIALOG(R)File 654:US Pat.Full.

02176464
Utility
BIOSENSORS INCLUDING LIPID BILAYER DOPED WITH ION CHANNELS ANCHORED TO A
RECORDING ELECTRODE BY BRIDGING MOLECULES

PATENT NO.: 5,204,239
ISSUED: April 20, 1993 (19930420)
INVENTOR(s): Gitler, Carlos, Rehovot, US (United States of America)
Yuli, Itzhak, Rehovot, IL (Israel)
ASSIGNEE(s): Yeda Research and Development Co Ltd , (A Non-U.S. Company or Corporation), Rehovot, IL (Israel)
[Assignee Code(s): 93576]
APPL. NO.: 7-638,488
FILED: January 09, 1991 (19910109)
PRIORITY: 93020, IL (Israel), January 9, 1990 (19900109)

FULL TEXT: 665 lines

ABSTRACT

Biosensors for qualitative and quantitative analysis comprise an amphipathic liquid crystalline membrane composed of a lipid bilayer attached to a recording electrode via bridging anchoring molecules. The lipid bilayer is doped with biologic or synthetic ion channels and is in continuous contact with a bulk aqueous medium on both its surfaces. The bridging anchoring molecules may contain a phospholipid moiety linked to a polyoxylakylene chain terminated with a thiol or thioether residue.

1/3,AB/14
DIALOG(R)File 654:US Pat.Full.

02010908
Utility
SEQUENTIAL PEPTIDE AND OLIGONUCLEOTIDE SYNTHESES USING IMMUNOAFFINITY
TECHNIQUES
[Capping]

PATENT NO.: 5,049,656
ISSUED: September 17, 1991 (19910917)
INVENTOR(s): Lewis, William, Lincoln, NE (Nebraska), US (United States of America)
Stout, Jay, Lincoln, NE (Nebraska), US (United States of America)
Van Heeke, Gino, Lincoln, NE (Nebraska), US (United States of America)
Wylie, Dwane E., Lincoln, NE (Nebraska), US (United States of America)
Schuster, Sheldon M., Lincoln, NE (Nebraska), US (United States of America)
Wagner, Fred W., Walton, NE (Nebraska), US (United States of America)
ASSIGNEE(s): Board of Regents of the University of Nebraska, (A U.S. Company or Corporation), Lincoln, NE (Nebraska), US (United States of America)
[Assignee Code(s): 58949]
APPL. NO.: 7-288,009
FILED: December 21, 1988 (19881221)

FULL TEXT: 862 lines

ABSTRACT

The invention is directed to a method for purifying sequentially synthesized peptides and oligonucleotides by immunoaffinity techniques. Selected products are lapped with an antigenic capping agent and are conjugated with antibodies that are specific for the capping agent.
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$16.56 Estimated cost File654
$16.56 Estimated cost this search
$82.41 Estimated total session cost 0.270 Hrs.
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=> t 1-4 cit ab kwic

1. 5,574,141, Nov. 12, 1996, Functionalized carrier materials for the simultaneous synthesis and direct labeling of oligonucleotides as primers for template-dependent enzymatic nucleic acid syntheses; Hartmut Seliger, et al., 536/22.1; 435/5, 6, 91.1, 91.2; 536/25.3 [IMAGE AVAILABLE]

US PAT NO: 5,574,141 [IMAGE AVAILABLE] L9: 1 of 4

ABSTRACT:

The synthesis and use of polymeric carriers is described which are loaded with nucleic acid building blocks which in turn contain labelling groups or precursors thereof. The polymeric carrier loaded in this way serves as a solid or liquid phase for the assembly of oligonucleotides which can be used as primers for template-dependent enzymatic nucleic acid syntheses such as for example in sequencing analysis according to Sanger and co-workers or in the polymerase chain reaction (PCR).

SUMMARY:

BSUM(13)

The . . . to the nucleoside anchored to the labelling phase which are able to impart a particular structural property to the oligonucleotide **synthesized** on this solid or liquid phase which is not inherent to the oligonucleotide chain itself. Non-radioactive labelling groups are preferred. These are preferably **fluorescent**, luminescent, antigenic or affinity-mediating groups and complex-forming groups. Furthermore these are also understood to include those groups, e.g. amino groups, which enable the attachment of a label, if necessary in a **protected** form. In a wider sense, those groups which as substituents of an oligonucleotide chain for example enable a possible therapeutic application of oligonucleotides by their capability of specifically binding or cleaving **DNA** or RNA [or proteins] should also be designated labelling groups within the scope of the invention. Particularly preferred labelling groups are **haptens** such as **fluorescein**, digoxigenin and biotin. **Haptens** are immunologically reactive chemical compounds with a molecular weight of less than 500 g/mol which do not themselves trigger an. . .

SUMMARY:

BSUM(17)

In . . . is preferably an amino group is reacted with a mononucleoside which is preferably activated at the 3' hydroxyl group and **protected** in the usual manner on the other reactive groups (e.g. 5' OH and primary amino groups of the nucleobases). This mononucleoside preferably has either a spacer with a terminal labelling group, preferably a reactive and **protected** group, on an amino group of the base or on an additional substituent attached to the base.

SUMMARY:

BSUM(19)

Subsequently the 5'-O-**protecting** groups (e.g. dimethoxytrityl) are cleaved from the labelling phase produced in this manner which preferably contains the **protected** mononucleoside bound via a spacer to the carrier material. Subsequently an oligonucleotide synthesis known from the state of the art. . .

SUMMARY:

BSUM(20)

After the synthesis, the labelled oligonucleotide chains are freed of **protecting** groups if necessary and cleaved from the polymers in such a way that the labelling groups or their precursors remain. . .

DETDESC:

DETD(3)

Synthesis of **Protected**, Labelled Nucleosides for Obtaining Labelling Phases

DETDESC:

DETD(34)

General Instructions for the Production of Labelling Phases for Oligonucleotide Synthesis Using Succinic Acid Esters of the **Protected** Labelled Nucleosides

DETDESC:

DETD(35)

The triethylammonium salt of the nucleoside succinate **protected** in a suitable manner (0.185 mmol, e.g. example 1 bc), a carrier material (1.0 g), N,N-dicyclohexylcarbodimine (200 mg, 1 mmol),. . .

DETDESC:

DETD(46)

Oligonucleotides . . . The pooled solution is concentrated to dryness in a Speed-vac evaporator. Anhydrous 2,2'-(ethylenedioxy)-diethylamine (100 .mu.l) is added to the partially **deprotected** oligonucleotides, the reaction vessel is closed and the oligonucleotide is dissolved at room temperature in an ultrasonic bath (5 to 10 min). The reaction solution is placed overnight in an incubator at 80.degree. C. The product which is completely **deprotected** with the exception of the p-toluenesulfonyl groups is precipitated from the amine solution. The reaction vessel is centrifuged and the. . .

2. 5,464,746, Nov. 7, 1995, Haptens, tracers, immunogens and antibodies for carbazole and dibenzofuran derivatives; James R. Fino, 435/6, 7.8; 536/26.6; 548/447 [IMAGE AVAILABLE]

US PAT NO: 5,464,746 [IMAGE AVAILABLE] L9: 2 of 4

ABSTRACT:
Novel tethered hapten intermediates and related conjugates based on carbazole and/or dibenzofuran, as well as methods for making and using such conjugates. Haptens based on the above core structures may be substituted at any position on the aromatic rings with a wide variety of substituents. Using tethered intermediates, immunogens, tracers, solid supports and labeled oligonucleotides are all described; as are methods for using the intermediates to prepare the conjugates, methods of using the conjugates to make and purify antibodies, as assay tracers, and in nucleic acid hybridization assays. Kits containing haptenated oligonucleotides and anti-hapten conjugates are also described.

SUMMARY:

BSUM(5)

According . . . for labeling an oligonucleotide, a label-phosphoramidite reagent is prepared and used to add the label to the oligonucleotide during its **synthesis**. For example, see Thuong, N. T. et al., Tet. Letters, 29(46):5905-5908 (1988); or Cohen, J. S. et al., U.S. patent application Ser. No. 07/246,688 (NTIS ORDER No. PAT-APPL-7-246,688) (1989). However, **DNA synthesis** reaction conditions are quite severe (e.g. iodine oxidation and ammonium hydroxide cleavage) and many **haptens** (e.g. biotin and **fluorescein**) do not readily withstand these conditions without modification. In another approach useful for labile **haptens**, a linker having a **protected** terminal amine is attached to the desired end of the oligonucleotide. The amine can be **deprotected** and, under milder conditions, reacted with a label.

SUMMARY:

BSUM(13)

In . . . di-(C.sub.1 -C.sub.10 -alkyl)amino, aryl-C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, halogen, amino, carboxy, carboxamido, hydroxy, mercapto, nitro, nitroso, sulfo, phospho and **protected** forms thereof; or alternatively a and a' when adjacent and

when taken together with the ca[redacted]s to which they are. . .

SUMMARY:

BSUM(14)

G . . . O, and NR wherein R is hydrogen, C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, optionally substituted sulfonyl, thiophenyl, carboxy, carboxamido, and **protected** forms thereof; and

DETDESC:

DETD(4)

For . . . di-(C.sub.1 -C.sub.10 -alkyl)amino, aryl-C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, halogen, amino, carboxy, carboxamido, hydroxy, mercapto, nitro, nitroso, sulfo, phospho and **protected** forms thereof; or alternatively a and a' when adjacent and when taken together with the carbons to which they are. . .

DETDESC:

DETD(5)

G . . . O, and NR wherein R is hydrogen, C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, optionally substituted sulfonyl, thiophenyl, carboxy, carboxamido, and **protected** forms thereof.

DETDESC:

DETD(17)

Protecting groups are defined as groups that can be removed under specific conditions, but which shelter or hide a reactive atom or functionality temporarily during intermediate reactions under other conditions. **Protecting** groups for hydroxyl, amino and thiol functionalities are well known in the art (T. W. Greene, **Protective** Groups in Organic Synthesis, John Wiley and Sons, NY, 1981). Hydroxyl functions are routinely **protected** as alkyl or aryl ethers alkyl, aryl, alkenyl), silyl ethers (silyl), esters (acyl), carbonates (C(.dbd.O)--O-alkyl, --C(.dbd.O)--O-aryl,--C(.dbd.O)--O-alkenyl) and carbamates (C(.dbd.O)-NH-alkyl,--C(.dbd.O)-NH-aryl, --C(.dbd.O)-NH-alkenyl). Amino functions are routinely **protected** as carbamates (--C(.dbd.O)--O-alkyl,--C(.dbd.O)--O-aryl,--C(.dbd.O)--O-alkenyl), amides (C(.dbd.O)-alkyl, --C(.dbd.O)-aryl,--C(.dbd.O)-alkenyl), cyclic imides (phthaloyl), N-benzyl derivatives (--CH.sub.(n) aryl.sub.(3-n), n=1-3), imine derivatives (.dbd.CH.sub.(n) alkyl.sub.(2-n), .dbd.CH.sub.(n) aryl.sub.(2-n). . . silyl derivatives (silyl), N-sulfenyl derivatives (S-aryl, --S--CH.sub.(n) aryl.sub.(3-n), n=0-3), and N-sulfonyl derivatives (-SO.sub.2 -aryl, -SO.sub.2 -alkyl). Thiol functions are routinely **protected** as thioethers (--CH.sub.(n) aryl.sub.(3-n), n= 1-3, alkyl), thioesters (acyl), thiocarbonates (C(.dbd.O)--O-alkyl,--C(.dbd.O)--O-aryl,--C(.dbd.O)--O-alkenyl), thiocarbamates (C(.dbd.O)-NH-alkyl,--C(.dbd.O)-NH-aryl,--C(.dbd.O)-NH-alkenyl), and disulfides (-S-alkyl, aryl). Where more than one **protecting** group is called for, it will be understood that each group may be independently selected from the various **protecting** groups. Indeed, one of ordinary skill in the art will know which **protecting** groups are routine for which functional groups.

DETDESC:

DETD(21)

Typically, . . . group consisting of hydroxy (--OH), thiol (--SH), carboxy (--C(.dbd.O)OH), amino (--NH.sub.2), aldehyde (--CH(.dbd.O)), leaving group, Michael acceptor, phosphoramidite, phosphonate and **protected** forms of these functional groups. In synthesis, the linking moiety often comprises a bifunctional compound designated x-L-y wherein x is. . .

DETDESC:

DETD(39)

The . . . L=--(CH.sub.2).sub.3 -- and y=CO.sub.2 C.sub.2 H.sub.5). The tether, -L-y thus becomes --O(CH.sub.2).sub.3 -CO.sub.2 C.sub.2 H.sub.5. The ethyl ester may be **deprotected** to a carboxylic acid by

saponification. The carboxylic a[redacted] is a reactive group capable of reacting with functional groups . . .

DETDESC:

DETD(70)

The . . . branching occurs only on carbon atoms; R.sup.1 and R.sup.10 are independently hydrogen, alkyl of from 1-10 carbon atoms, an amino **protecting** group, or aryl, alternatively R.sup.1 or R.sup.10 when taken together with W and the nitrogen atom to which they are. . . be done very slowly to avoid a dangerously fast release of gas. The primary hydroxyl of the diol is then **protected** by dimethoxytritylation (step 5) to form the tethered hapten 5. The tethered hapten is then phosphoramidated at the secondary alcohol. . .

DETDESC:

DETD(99)

Carbazole . . . minutes. The reaction was allowed to come to ambient temperature then heated at 40.degree. C. for 18 h, under N.sub.2, **protected** from light. The solvent was removed under reduced pressure and the residue taken up in glyme (60 mL) and aqueous. . .

DETDESC:

DETD(111)

N-t-BOC--O-(2-aminoethyl)-2-aminoethanol . . . residue purified by column chromatography using ethyl acetate/hexanes as the eluant. Mass spectrum: DCI/NH.sub.3, (m+H).sup.+ @ m/z 456. The BOC **protecting** group was removed with trifluoroacetic acid/dichloromethane (5 mL, 1:1) giving the trifluoroacetate salt of the amine.

DETDESC:

DETD(121)

Carbazole-diol . . . diisopropylethylamine (4.5 mL, 33.7 mmole), and N,N-dimethylaminopyridine (0.16 g, 1.3 mmole) were added. The reaction was stirred under nitrogen atmosphere, **protected** from light, for 18 h at ambient temperature. The solvent was removed in vacuo and the residue purified by flash. . .

DETDESC:

DETD(124)

The . . . CaH) and 2-cyanoethyl N,N-diisopropylchlorophosphoramidite (3.1 mL, 14 mmole) were added. The reaction was kept at ambient temperature, under nitrogen atmosphere, **protected** from light for 2 h. Dry methanol (0.6 mL) was added and then after 20 min ethyl acetate (200 mL). . .

DETDESC:

DETD(140)

The . . . one part was added a small amount of 5-AMF and a drop of DIEA. After 72 h at ambient temperature, **protected** from light, the reaction was purified using preparative TLC (reverse phase, C18, 1000 .mu.m plates, methanol/500 mM NaCl, 6:4) giving. . .

DETDESC:

DETD(142)

To . . . (G57) is added a small amount of N-glycylfluoresceinamine and a drop of DIEA. After about 72 h at ambient temperature, **protected** from light, the reaction is purified using preparative TLC (reverse phase, C18, 1000 .mu.m plates, methanol/500 mM NaCl, 6:4) giving. . .

DETDESC:

DETD(144)

The . . . one part was added mall amount of 5-AMF and a drop of DIEA. After 72 h at ambient temp ure, **protected** from light, the reaction was purified using preparative TLC (reverse phase, C18, 1000 .mu.m plates, methanol/500 mM NaCl, 6:4) giving. . .

DETDESC:

DETD(146)

To . . . (G58) is added a small amount of N-glycylfluoresceinamine and a drop of DIEA. After about 72 h at ambient temperature, **protected** from light, the reaction is purified using preparative TLC (reverse phase, C18, 1000 .mu.m plates, methanol/500 mM NaCl, 6:4) giving. . .

DETDESC:

DETD(150)

Dbf-BAE . . . (0.012 mL, 0.067 mmol) are added as in examples 17 and 19 above. After about 18 h at ambient temperature, **protected** from light, the solvent is removed under reduced pressure and the residue purified by preparative TLC (reversed phase C18, 1. . .

CLAIMS:

CLMS(1)

What . . .

di-(C.sub.1 -C.sub.10 -alkyl)amino, aryl-C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, halogen, amino, carboxy, carboxamido, hydroxy, mercapto, nitro, nitroso, sulfo, phospho and **protected** forms thereof; or

G is selected from S, O, and NR wherein R is hydrogen, C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, optionally substituted sulfonyl, thiophenyl, carboxy, carboxamido, and **protected** forms thereof;

A is a linking moiety of the formula -L-y, wherein y is a functional group that can react directly. . .

CLAIMS:

CLMS(2)

2. The conjugate according to claim 1 wherein a is hydrogen and a' is amino, halogen, hydroxy, nitro, and **protected** forms thereof.

CLAIMS:

CLMS(3)

3. . . . group consisting of hydroxyl (--OH), thiol (--SH), carboxy (--C(.dbd.O)OH), amino (--NH.sub.2), aldehyde (--CH(.dbd.O)), leaving group, Michael acceptor, phosphoramidite, phosphonate and **protected** forms of these functional groups.

CLAIMS:

CLMS(5)

5. . . . 4 wherein a is hydrogen and a' is selected from the group consisting of hydrogen, amino, halogen, hydroxy, nitro, and **protected** forms thereof.

3. 5,424,414, Jun. 13, 1995, Haptens, tracers, immunogens and antibodies for 3-phenyl-1-adamantaneacetic acids; Philip G. Mattingly, 536/25.32; 560/102 [IMAGE AVAILABLE]

US PAT NO: 5,424,414 [IMAGE AVAILABLE] L9: 3 of 4

ABSTRACT:
Novel tethered hapten intermediates and related conjugates based on 3-phenyl-1-adamantaneacetic acid, as well as methods for making and using such conjugates. Haptens based on the above core structure may be substituted at any position on the phenyl ring, especially at the para position. Using tethered intermediates, immunogens, tracers, solid supports and labeled oligonucleotides are all described; as are methods for using the intermediates to prepare the conjugates, methods of using

the conjugates to make and purify anitbodies, as assay tracers, and in nucleic acid hybridization assays. Kits containing haptenated oligonucleotides and anti-hapten conjugates are also described.

SUMMARY:

BSUM(5)

According . . . for labeling an oligonucleotide, a label-phosphoramidite reagent is prepared and used to add the label to the oligonucleotide during its **synthesis**. For example, see Thuong, N. T. et al., Tet. Letters, 29(46):5905-5908 (1988); or Cohen, J. S. et al., U.S. patent application Ser. No. 07/246,688 (NTIS ORDER No. PAT-APPL-7-246,688) (1989). However, **DNA synthesis** reaction conditions are quite severe (e.g. iodine oxidation and ammonium hydroxide cleavage) and many **haptens** (e.g. biotin and **fluorescein**) do not readily withstand these conditions without modification. In another approach useful for labile **haptens**, a linker having a **protected** terminal amine is attached to the desired end of the oligonucleotide. The amine can be **deprotected** and, under milder conditions, reacted with a label.

SUMMARY:

BSUM(12)

In . . . -C.sub.10 -alkyl)amino, aryl- C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, halogen, amino, carboxy, carboxamide hydroxy, mercapto, nitro, nitroso, sulfo, phospho and **protected** forms thereof; or

DETDESC:

DETD(16)

Protecting groups are defined as groups that can be removed under specific conditions, but which shelter or hide a reactive atom or functionality temporarily during intermediate reactions under other conditions. **Protecting** groups for hydroxyl, amino and thiol functionalities are well known in the art (T. W. Greene, **Protective** Groups in Organic Synthesis, John Wiley and Sons, N.Y., 1981). Hydroxyl functions are routinely **protected** as alkyl or aryl ethers alkyl, aryl, alkenyl), silyl ethers (silyl), esters (acyl), carbonates (C(.dbd.O)--O-alkyl, --C(.dbd.O)--O-aryl, --C(.dbd.O)--O-alkenyl) and carbamates (C(.dbd.O)--NH-alkyl, --C(.dbd.O)--NH-aryl, --C(.dbd.O)--NH-alkenyl). Amino functions are routinely **protected** as carbamates (--C(.dbd.O)--O-alkyl, --C(.dbd.O)--O-aryl, --C(.dbd.O)--O-alkenyl), amides (C(.dbd.O)-alkyl, --C(.dbd.O)-aryl, --C(.dbd.O)-alkenyl), cyclic imides (phthaloyl), N-benzyl derivatives (--CH.sub.(n) aryl.sub.(3-n), n=1-3), imine derivatives (.dbd.CH.sub.(n). . . derivatives (silyl), N-sulfenyl derivatives (S -aryl, --S--CH.sub.(n) aryl.sub.(3-n), n=0-3), and N-sulfonyl derivatives (--SO.sub.2 -aryl, --SO.sub.2 -alkyl). Thiol functions are routinely **protected** as thioethers (--CH.sub.(n) aryl.sub.(3-n), n=1-3, aklyl), thioesters (acyl), thiocarbonates (C(.dbd.O)--O-alkyl, --C(.dbd.O)-O-aryl, --C(.dbd.O)--O-alkenyl), thiocarbamates (C(.dbd.O)--NH-alkyl, --C(.dbd.O)-NH-aryl, --C(.dbd.O)--NH-alkenyl), and disulfides (--S-alkyl, aryl). Where more than one **protecting** group is called for, it will be understood that each group may be independently selected from the various **protecting** groups. Indeed, one of ordinary skill in the an will know which **protecting** groups are routine for which functional groups.

DETDESC:

DETD(20)

Typically, . . . group consisting of hydroxy (--OH), thiol (--SH), carboxy (--C(.dbd.O)OH), amino (--NH.sub.2), aldehyde (--CH(.dbd.O)), leaving group, Michael acceptor, phosphoramidite, phosphonate and **protected** forms of these functional groups. In synthesis, the linking moiety often comprises a bifunctional compound designated x--L--y wherein x is. . .

DETDESC:

DETD(31)

Haptens . . . and a' when taken alone are 1-5 groups independently selected from the group consisting of: hydrogen (H), alkyl, amino (--NH.sub.2), **protected** amino [--N(H).sub.n Z, n=0-1 to satisfy valency and Z is a **protecting** group], aryl, carboxy (--CO.sub.2 H), **protected** carboxy (--CO.sub.2 Z), carboxamido (--C(.dbd.O)NRR', R and R' independently are H, alkyl or aryl, halo (--F, --Cl, --Br, --I), hydroxy (--OH), **protected** hydroxy (--OZ), mercapto (--SH), **protected** mercapto (--SZ), nitro (--NO.sub.2), nitroso (--NO), sulfo (--SO.sub.3 -), and phospho (--PO.sub.3.sup.-2); and wherein further, any two adjacent substituents may. . .

DETDESC:

DETD(34)

wherein B is selected from the group consisting of -hydroxy (--OH), **protected** hydroxy, amino (--NR"R'", where R" and R'" may independently be H, alkyl or aryl), thiol (--SH), **protected** thiol, and a leaving group. The **protecting** groups (where more than one are present) may be the same or different and may be selected from among the many known **protecting** groups for O, N and/or S.

DETDESC:

DETD(43)

The . . . group consisting of hydroxy (--OH), thiol (--SH), carboxy (--C(.dbd.O)OH), amino (NH.sub.2), aldehyde (--CH(.dbd.O)), leaving group, Michael acceptor, phosphoramidite, phosphonate and **protected** forms of these functional groups to form the tethered intermediate (II).

DETDESC:

DETD(73)

Scheme I (See FIG. 1) begins with the synthesis of the tether. The starting compound is an amino-**protected** carboxylate 1 wherein W is a spacer group of from 1 to about 50 atoms arranged in a straight or. . . branching occurs only on carbon atoms; R.sup.1 and R.sup.10 are independently hydrogen, alkyl of from 1-10 carbon atoms, an amino **protecting** group, or aryl, alternatively R.sup.1 or R.sup.10 when taken together with W and the nitrogen atom to which they are. . . (step 4) with sodium borohydride under reflux conditions to the diol 4. The primary hydroxyl of the diol is then **protected** by dimethoxytritylation (step 5). The amino is then N-**deprotected** (step 6) to 5 which is reacted with hapten 6 to form the tethered hapten 7. The tethered hapten is. . .

DETDESC:

DETD(99)

. . .

a fluorophore

BAE 3 carboxypropyloxy radical

BSA Bovine Serum Albumin, an immunogenicity conferring carrier.

Cbz Carbonylbenzyloxy, an amino **protecting** group

Celite .RTM. A trademark of Manville Products Corporation, for diatomaceous earth

CDI 1,1'carbonyldiimidazole, a coupling reagent

DCC. . .

DETDESC:

DETD(126)

B. The intermediate **protected** compound was dissolved in methylene chloride (10 mL, anhydrous) and treated with TFA (1 mL) at 0.degree. C. under nitrogen. . .

DETDESC:

DETD(129)

B. The intermediate **protected** compound was dissolved in refluxing methanol (200 mL) containing sodium hydroxide (3.18 g, 79.6 mmoles) and water (20 mL). Reflux. . .

CLAIMS:

CLMS(1)

What . . .

-C.sub.10 -alkyl)amino, aryl-C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, halogen, amino, carboxy, carboxamido, hydroxy, mercapto, nitro, nitroso, sulfo, phospho and **protected** forms thereof; or
alternatively a and a' when taken together with the carbons to which they are joined form a. . .

CLAIMS:

CLMS(2)

2. . . . di-(C.sub.1 -C.sub.10 -alkyl)amino, aryl-C.sub.1 -C.sub.10 -alkyl, optionally substituted aryl, halogen, amino, carboxy, carboxamido, hydroxy, mercapto, nitro, nitroso, sulfo, phospho and **protected** forms thereof.

4. 5,290,925, Mar. 1, 1994, Methods, kits, and reactive supports for 3' labeling of oligonucleotides; James R. Fino, 536/25.32; 435/6; 501/33; 524/1 [IMAGE AVAILABLE]

US PAT NO: 5,290,925 [IMAGE AVAILABLE] L9: 4 of 4

ABSTRACT:
In a first aspect, the invention involves a reactive support useful for automated synthesis of oligonucleotides. The reactive support comprises a label moiety (e.g. hapten) covalently bonded via a stable bond to a trifunctional spacer. The labeled trifunctional spacer complex is covalently bonded to a solid support via a cleavable bond. One arm of the trifunctional spacer attaches the solid phase; another arm attaches the label; while the third arm provides a hydroxyl group useful for synthesizing a labeled oligonucleotide. Upon synthesis, the cleavable bond is broken, yielding the labeled oligonucleotide. Methods for labeling oligonucleotides and useful kits are also described.

SUMMARY:

BSUM(8)

Nelson, . . . a control pore glass solid support having incorporated therein a multifunctional agent having both a masked amino group and a **protected** hydroxyl group. The hydroxyl group can be used for standard synthesis of oligonucleotides as is known in the art. The **protected** amino group can be used after synthesis and cleavage of the oligonucleotide for coupling to a reporter molecule. This approach. . .

SUMMARY:

BSUM(12)

In . . . integers from 1 to about 30; p is an integer from 0 to about 30; G is H or a **protecting** group; and Z is a linking group having a cleavable bond.

SUMMARY:

BSUM(15)
a. providing a trifunctional linker with three functionalities, a first one of whose functionalities is a hydroxyl group or a **protected** hydroxyl group and each of whose functionalities has or can be made to have a differential reactivity;

SUMMARY:

BSUM(18)

The . . . integers from 1 to about 30; p is an integer from 0 to about 30; G is H or a **protecting** group; and X and Y are independently selected from the group consisting of hydroxyl, amino, thiol and carboxyl. Preferably, n. . .

SUMMARY:

BSUM(19)

In . . . end of an oligonucleotide synthesized on a solid support is described. The method includes preparing a reactive support having a **protected** hydroxyl group according to the above method, followed by **deprotecting** the hydroxyl group and synthesizing an oligonucleotide from the **deprotected** hydroxyl group. Preferably, the oligonucleotide is synthesized by known, automated methods.

SUMMARY:

BSUM(20)

Finally, . . . detectable marker or to a solid phase. Preferably, the detectable marker is an enzyme label. Optionally, the kit may include **protected** nucleic acid phosphoramidite reagents necessary for DNA synthesis.

SUMMARY:

BSUM(23)

The . . . a linking group having a cleavable bond; TF represents a trifunctional spacer as described below; G is H or a **protecting** group; and LABEL represents the detectable label moiety, preferably a hapten.

SUMMARY:

BSUM(24)

More . . . integers from one to about 30; p is an integer from 0 to about 30; G is H or a **protecting** group; and Z is a linking group having a cleavable bond. Preferably, integers m and n are between 1 and. . .

SUMMARY:

BSUM(25)

A . . . molecule. A trifunctional linker is a reagent having three reactive functionalities, wherein a first one of the functionalities is a **protected** hydroxyl group and each of the three functionalities has or can be made to have a differential reactivity. The term. . . is used when two of the reactive functionalities of the linker have been reacted with other molecules, leaving only the **protected** hydroxyl group (which is used for synthesis of an oligonucleotide).

SUMMARY:

BSUM(35)

In the present invention, **haptens** are the preferred label moieties. These can be detected by specific binding partners such as antibodies which have been coupled to detectable markers such as enzymes. Exemplary **haptens** include biotin, **fluorescein**, dansyl and many others. Virtually any compound which can be made to elicit an immune response to form antibodies can be used as a **hapten** in the present invention, provided it is stable to the relatively harsh conditions of **nucleic** acid **synthesis**. These conditions have been described in detail in the literature, but briefly comprise an acidic detritylation step, an oxidation step, and a basic base **deprotection** step.

SUMMARY:

BSUM(36)

Preferably, a **protecting** group prevents the first functionality from reacting in undersirable situations. This procedure is well known to those of skill in this art to preserve a hydroxyl group for subsequent synthesis of DNA or other oligonucleotides. Suitable **protecting** groups include dimethoxytrityl (DMT), monomethoxytrityl (MMT), tetrahydropyranyl (THP) and substituted THP, 2 methoxyethoxymethyl (MEM) and substituted ethyl ethers such as. . .

SUMMARY:

BSUM(43)

At least a first one of the reactive functionalities is a hydroxyl o
protected hydroxyl group which ultimately serves as the basis for automated DNA synthesis. Generally, the remaining reactive functionalities will include hydroxyl,. . .

SUMMARY:

BSUM(44)
. . .
Y
GROUP, X
(primary)
(secondary)
Note

--OH	--OH	provided the first hydroxyl (primary OG) is **protected**, or otherwise differentiable from the second primary alcohol, Y
--OH	--NH.sub.2	provided the first hydroxyl (primary OG) is **protected**, or otherwise differentiable from the second primary alcohol, Y
--OH	--COOH	provided the first hydroxyl (primary OG) is **protected**, or otherwise differentiable from the second primary alcohol, Y
--NH.sub.2	--OH	
--NH.sub.2	--NH.sub.2	
--NH.sub.2	--SH. . .	

SUMMARY:

BSUM(48)

The . . . bond. The linking group including its cleavable bond, is generally added next. Of course, the final functionality will remain a **protected** hydroxyl group and is used for subsequent synthesis of a nucleic acid to which the label will be attached at. . .

SUMMARY:

BSUM(49)

It will be understood by those of ordinary skill in this art, that intermediate **protecting** and **deprotecting** steps may be required although they have not been set forth in detail herein. **Protecting** groups may be required to achieve the differential reactivity required of the invention. For example, a triol trifunctional linker (e.g.. . . secondary) is possible if one can differentiate the two primary hydroxyls. Example 1 shows one method of achieving this. Conventional **protecting** groups such as DMT or MMT may also be required to preserve the hydroxyl group necessary for oligonucleotide synthesis.

SUMMARY:

BSUM(50)

Having . . . solid support is added to the instrument along with the requisite nucleic acid phosphoramidite reagents. If the support contains a **protecting** group on the hydroxyl, as is preferred, the first step will be the removal of the **protecting** group. Using the available hydroxyl, DNA is synthesized according to the manufacturer's instructions. Upon completion of synthesis, the support is. . .

DETDESC:

DETD(5)

A . . . 10% sodium carbonate (20 mL). After the addition, the ice bath was removed and the reaction stirred at room temperature, **protected** from light, for 18 h. The reaction utilizes the amino functionality to give a labeled diol product, which was extracted. . .

DETDESC:

DETD(7)

Dansyl-diol . . . room temperature for 18 h then the solvent was removed under reduced pressure. The product (labeled trifunctional linker having a **protected** primary hydroxyl) was purified by flash chromatography, eluting with 2:8, ethyl acetate/hexanes. The solvent was removed giving a yellow glass. . .

CLAIMS:

CLMS(1)

What is claimed is:

1. A reactive support having a free or **protected** hydroxyl group useful for synthesis of an oligonucleotide, said support comprising a label moiety covalently bonded via a stable bond. . .

CLAIMS:

CLMS(2)

2. . . . integers from 1 to about 30; p is an integer from 0 to about 30; G is H or a **protecting** group; and Z is a linking group having a cleavable bond.

CLAIMS:

CLMS(10)

10. A reactive support having a free or **protected** hydroxyl group useful for synthesis of an oligonucleotide, said support comprising a label moiety covalently bonded via a stable bond. . .

CLAIMS:

CLMS(11)

11. . . .
functionality of a trifunctional linker having three functionalities, a first one of whose functionalities is a hydroxyl group or a **protected** hydroxyl group and each of whose functionalities has or can be made to have a differential reactivity, with a label. . .

CLAIMS:

CLMS(16)

16. . . . integers from 1 to about 30; p is an integer from 0 to about 30; G is H or a **protecting** group; and X and Y are independently selected from the group consisting of hydroxyl, amino, thiol and carboxyl.

CLAIMS:

CLMS(20)

20. . . .
a. reacting the second functionality of a trifunctional linker having three functionalities, a first one of whose functionalities is a **protected** hydroxyl group and each of whose functionalities has or can be made to have a differential reactivity, with a label. . . solid support under conditions such that the trifunctional linker is covalently attached to the solid support via the cleavable bond.
c. **deprotecting** the hydroxyl group; and
d. synthesizing an oligonucleotide from the **deprotected** hydroxyl